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Autism spectrum disorder and attention-deficit/hyperactivity disorder in early childhood:

A review of unique and shared characteristics and developmental antecedents

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Highlights

- Connects research on early symptoms, temperament and cognition in ASD and ADHD.
- Examines composite domains or factors as well as subdomains and basic components.
- Provides explanations for the lower ASD-ADHD co-occurrence under the age of three.
- Provides explanations for increase in executive dysfunction with preschool age.
- Attention problems may be a common pathway to ASD and ADHD.
- Proposes a motivational model for temperament differences between ASD and ADHD.
- Low effortful control may have different underpinnings in ASD and ADHD.
- Discusses the role of executive function in the pathways to ASD and ADHD.

Abstract

Autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) have overlapping characteristics and etiological factors, but to which extent this applies to infant- and preschool age is less well understood. Comparing the pathways to ASD and ADHD from the earliest possible stages is crucial for understanding how phenotypic overlap emerges and develops. Ultimately, these insights may guide preventative and therapeutic interventions. Here, we review the literature on the core symptoms, temperament and executive function in ASD and ADHD from infancy through preschool age, and draw several conclusions: (1) the co-occurrence of ASD and ADHD increases with age, severity of symptoms and lower IQ, (2) attention problems form a linking pin between early ASD and ADHD, but the behavioral, cognitive and sensory correlates of these attention problems partly diverge between the two conditions, (3) ASD and ADHD share high levels of negative affect, although the underlying motivational and behavioral tendencies seem to differ, and (4) ASD and ADHD share difficulties with control and shifting, but partly opposite behaviors seem to be involved.

Keywords: ASD, ADHD, autism, infant, preschool age, attention, temperament, executive function, early developmental pathways, early developmental mechanisms.

1. Introduction

ASD and ADHD are neurodevelopmental disorders that share an early onset, delays and deviances in the development of brain structure/function, cognitive impairments, a male preponderance, and strong genetic influences on individual differences and liability (Rutter, Kim-Cohen, & Maughan, 2006). Over the past decade, research has indicated that symptoms of ASD and ADHD frequently co-occur in the same individuals and cluster within families (de Bruin, Ferdinand, Meester, de Nijs, & Verheij, 2007; Melegari et al., 2015; Simonoff et al., 2008) (Hofvander et al., 2009; Lundstrom et al., 2011). Further, both conditions have overlapping characteristics and etiological factors (see Posthuma & Polderman, 2013; Rommelse, Franke, Geurts, Hartman, & Buitelaar, 2010; Rommelse, Geurts, Franke, Buitelaar, & Hartman, 2011; Ronald, Pennell, & Whitehouse, 2010; Taurines et al., 2012 for reviews). However, most of this research has been conducted in middle childhood and early adolescence. To which extent ASD and ADHD overlap or differ at the level of overt characteristics, brain mechanisms and etiology at infant and preschool age is less well understood.

There are important reasons for studying the development of ASD and ADHD and their phenotypic overlap from the earliest possible stages. Both ASD and ADHD, like most psychopathological conditions, develop from interactions among multiple genetic and environmental influences on a network of neurobiological systems that begin to unfold in prenatal life (Rutter, 2011; Sonuga-Barke & Halperin, 2010). These interactions explain why distinct impairments and risks in ASD and ADHD show varied developmental trajectories and outcomes (see (Elsabbagh et al., 2011; Sonuga-Barke, 2005; Thapar, Cooper, Eyre, & Langley, 2013; Willcutt et al., 2012) for reviews). Studying the associations between ASD and ADHD in the first years of life makes it possible to examine whether and how phenotypic overlap emerges and develops, and whether the development of one disorder or dysfunction leads to the development of the other(s); or alternatively, whether distinct disorders or dysfunctions originate from a common set of early risk factors. Further, study at very young age may allow the identification of the behavioral, cognitive, neural, genetic and environmental processes that precede/ underlie the expression of

clinical symptoms of ASD and ADHD. Ultimately, insight in these early processes may have implications for preventative and therapeutic interventions (Sonuga-Barke & Halperin, 2010; Yirmiya & Charman, 2010).

Here, we review the literature on the early signs and developmental antecedents of ASD and ADHD. We focus on the core behaviors, temperament and cognition in children up to preschool age and highlight the unique and shared characteristics of both conditions. Doing so, we partly build on a recent review focusing on early markers for ASD and ADHD in infants at risk (Johnson, Gliga, Jones, & Charman, 2014). Up till now, research in ASD has an obvious lead over ADHD as regards the precursors and early signs and has recently been discussed in four reviews (Elsabbagh & Johnson, 2010; Jones, Gliga, Bedford, Charman, & Johnson, 2014; Yirmiya & Charman, 2010; Zwaigenbaum, Bryson, & Garon, 2013). There is only one review explicitly comparing the early characteristics of ASD and ADHD (M. H. Johnson et al., 2014); Our review adds to this review (1) by including not only studies with children at familial risk but also studies with clinical and population samples, allowing to examine the characteristics in a wider range of severity of ASD and/or ADHD, (2) by an in depth focus on the core symptoms, temperament and early emerging executive function in ASD versus ADHD. This is relevant as co-morbidity may be a result of interactions among such characteristics over time, conform a network approach to disorders and co-morbidity (Borsboom & Cramer, 2013; Borsboom, Cramer, Schmittmann, Epskamp, & Waldorp, 2011) instead of being merely a result of latent constructs, (3) by extending the age range to preschool years (up to 7) in contrast to previous reviews. This is of particular relevance since many characteristics, in particular neurocognitive capacities, while emerging in the first months of life, continue to undergo important changes during the 3rd to 6th year. We chose for a qualitative review approach because of the inclusion of a wide range of data on ASD and ADHD from a disparate literature that does not lend itself to a quantitative pooling of results, in line with the directives for reviews highlighted by (Nigg, 2012).

Several issues that explain the approach and focus of the present review warrant consideration. First, ASD and ADHD are both heterogeneous conditions. Symptoms of ASD and ADHD range from mild

and even subclinical traits in the general population to fully developed clinical disorders (Coghill & Sonuga-Barke, 2012; Constantino, 2011; Frazier, Youngstrom, & Naugle, 2007; Lubke, Hudziak, Derks, van Bijsterveldt, & Boomsma, 2009). As similar heritability estimates have been found across different levels of severity in ASD and in ADHD (Larsson, Anckarsater, Rastam, Chang, & Lichtenstein, 2012; Robinson et al., 2011), similar etiologic factors may operate along the continuum of severity. Therefore, we include both studies reporting on subclinical, quantitative traits as well as clinical symptoms of ASD and ADHD. Second, both ASD and ADHD encompass distinct core symptom domains with (partly) differing heritability and course. In ASD these domains are the social-communicative versus restrictive-repetitive behavior domains (Happe & Ronald, 2008; Robinson et al., 2012), and in ADHD the hyperactivity-impulsivity versus inattention domains (Frazier et al., 2007; Greven, Asherson, Rijsdijk, & Plomin, 2011; Greven, Rijsdijk, & Plomin, 2011; Nikolas & Burt, 2010). Third, valid assessment of early signs in the core domains of ASD and ADHD is compromised by the uneven maturational course of different skills and corresponding impairments (Pauli-Pott & Becker, 2011, 2015). Specifically, several core symptoms of ASD generally manifest at an earlier age than the core symptoms in ADHD. ASD may reliably be diagnosed from about the second year (Yirmiya & Charman, 2010; Zwaigenbaum et al., 2013), whereas the first signs of ADHD show much overlap with ubiquitous ADHD-like behaviors and only become predictive of ADHD from about preschool age onwards (Leblanc et al., 2008; Sonuga-Barke & Halperin, 2010; Wahlstedt, Thorell, & Bohlin, 2008). This is why early emerging dysfunctions like those in attentional processes, and temperamental traits are of particular interest in very young children as these may represent more direct risk markers of atypical development than later emerging clinical phenotypes (Elsabbagh et al., 2011; Elsabbagh & Johnson, 2010; Gurevitz, Geva, Varon, & Leitner, 2012; Nigg, Goldsmith, & Sachek, 2004). Alternatively, early emerging dysfunctions may act as modifiers of the phenotype and developmental course of ASD and ADHD (Clifford et al., 2013; Johnson, 2012; Mundy, Henderson, Inge, & Coman, 2007). Hence, in this review we take into consideration behavioral measures belonging to the core domains as well as measures of temperamental and cognitive domains.

2. Method

2.1. Identification of studies

We searched with *PubMed* and *Web of Science* for peer reviewed English-language research articles published between 2000 and February 2015. The following search terms were used: autism (spectrum) (disorder), ASD, attention deficit (hyperactivity) (disorder), and ADHD in combinations with: co-morbidity, attention (deficit), hyperactivity, impulsivity, social (communication), repetitive behavior, cognition, neuropsychology, executive function, temperament, effortful control, at (high-)risk, early markers, infant, toddler, preschool. References given in the selected publications were screened for further relevant articles.

As few studies with very young children have directly compared ASD and ADHD, we will also evaluate findings in ASD and ADHD separately. For our purpose, several study designs in very young children are of interest: 1) cross-sectional and longitudinal studies on the associations between autistic and ADHD traits or symptoms in community or clinical samples; 2) cross-sectional and longitudinal studies on cognitive or temperamental characteristics in children who scored high on ASD and/or ADHD symptoms or who had a clinical ASD and/or ADHD diagnosis; and 3) prospective longitudinal studies in high-risk children (i.e., first degree relatives of individuals with ASD or ADHD) focusing on early behavioral, cognitive and temperamental signs.

For research on the developmental antecedents of disorders, prospective longitudinal studies are the most informative. These may shed light on the continuities and discontinuities in the separate domains/characteristics and on their interactions. Here, prospective high-risk (HR) studies have additional advantages in highly heritable disorders such as ASD and ADHD. High-risk studies are based on children at familial risk for developing the condition. The study of HR siblings during the first years of life and before the onset of clinically diagnosable symptoms, may reveal primary processes leading to symptom emergence before these are confounded by compensatory/secondary mechanisms (M. H. Johnson et al., 2014). Moreover, studying at-risk siblings who continue to be unaffected might illuminate protective factors. HR studies require relatively small samples by ensuring high rates of the (precursor) core

characteristics and of subclinical traits that may be present in relatives of individuals with ASD and/or ADHD. Ideally, a low risk group serves as control. We also included the few HR studies in ADHD, generally based on high ADHD scores in children's fathers, even if the child's own diagnostic status was unknown. Clinical studies also ensure high rates of the characteristics of interest, but do not provide direct information on the developmental antecedents prior to diagnosis and on subclinical traits, and may thus be subject to participant bias. Despite these limitations, clinical studies in young children, either cross-sectional or longitudinal, provide valuable and detailed information on the early core symptoms and related domains of impairment. Study designs in representative populations minimize the risk of participant bias, but require very large samples to ensure sufficient rates of the characteristics under investigation. To overcome this disadvantage population based "enriched" subsamples are currently used, resulting from enrolment after screening for the characteristics of interest. Retrospective study designs finally, in particular home video studies wherein blind observations of film material has occurred, allow for the evaluation of naturally occurring behaviors long before diagnosis but are biased by non-standardized procedures (Yirmiya & Charman, 2010). In the absence of comparable studies in ADHD, we did not include retrospective home video studies in this review.

This review is organized in subsections that focus on findings in the behavioral, temperamental and cognitive domains. We acknowledge that the frameworks we use for these domains may not exactly correspond with the traits and measures used in the reviewed literature, a limitation that we will consider when discussing the different domains. To better ensure comparability between studies, we therefore report on the results at item or sub-trait level if possible. For each behavioral, temperamental and cognitive domain we briefly describe the concepts on which we compare the disorders, summarize the ASD and ADHD literature, and then examine the overlap and specificity of findings. In the discussion, we first consider the implications of reviewed findings for theories on the early pathways of ASD and ADHD. Secondly, we discuss the challenges presented by the diverging research fields of ASD and ADHD and by the substantial developmental changes during early childhood. We conclude with recommendations for future research.

2.2. Inclusion criteria

To be included in this review, a study had to meet each of the following requirements: a) assessment of ASD and/or ADHD symptoms or traits, and ASD and/or ADHD symptoms have been defined using standardized instruments; b) assessment of participants younger than six years at the start of the study. Longitudinal studies following children beyond their seventh year and studies including older children were reviewed if data were reported separately for children up to seven years of age; c) assessment of correlates and predictor variables using standardized and validated measures; d) including community and/or clinical samples, and adopting a dimensional approach to autistic and/or ADHD traits or symptoms, or based on categorical ASD and/or ADHD diagnoses; and e) using cross-sectional or longitudinal designs. Studies on high-risk samples were only included if they reported on outcome data and/or included a low risk control group. Studies only based on retrospective data were excluded.

3. Core behavioral characteristics

The co-occurrence of ASD and ADHD symptoms or traits in early childhood has been investigated using two different approaches, by examining either the pairwise associations between DSM-defined full diagnoses of ASD and ADHD, or the presence of symptoms or traits of ASD and/or ADHD in clinical or population based samples (see Table Appendix 1., for a summary of included studies).

3.1. Co-morbidity between ADHD and ASD diagnoses

The frequency of co-morbid ASD and ADHD diagnoses in children younger than 7 years old has only been investigated in ASD samples. Three of these studies have used parent questionnaires to confer DSM-IV based ADHD diagnoses (Gadow, DeVincent, Pomeroy, & Azizian, 2004; Lecavalier, Gadow, Devincent, Houts, & Edwards, 2011; Turygin, Matson, & Tureck, 2013), and one study has used parent reports of diagnosed ADHD or severe hyperactivity (Carlsson et al., 2013). In an ASD subgroup of a mixed clinical and special education sample of 3-5 year old children over 40% met criteria for ADHD (Gadow et al., 2004), and in an early ASD intervention sample of 4.6-5.6 year old children 32% had diagnosed ADHD

or severe hyperactivity (Carlsson et al., 2013). In comparison, an overall ADHD prevalence of just 4.5% was reported in the ASD subgroup aged 2.1 years from an early intervention sample (Turygin et al., 2013). Such varying ADHD reports may be explained by the age differences across studies. It is known that ADHD symptoms become more manifest and better differentiable from normative behaviors *after* toddlerhood (Sonuga-Barke & Halperin, 2010). Further, studies differ as to whether more or less stringent criteria for ADHD were used. For example, in Turygin et al. (2013) parents rated their child's ADHD symptoms in relation to same-aged peers, making judgements of whether the child was ''different'' or ''very different'' from same-aged peers, instead of being based on the mere presence of ADHD symptoms (Gadow et al., 2004), or on previous ADHD diagnoses or severe hyperactivity (Carlsson et al., 2013). In addition, psychiatrically referred children with ASD (Gadow et al., 2004) may show more severe psychiatric symptoms like ADHD than the ASD subsample of children referred to an early intervention program for children with a developmental delay in Turygin et al. (2013).

Regarding the significance of co-morbid ADHD, it is unclear whether ADHD symptoms observed in ASD at young age refer to the same constructs as in typical ADHD without ASD. To shed light on this issue the factor structure of ADHD symptoms in ASD was examined. In the abovementioned study with 3-5 year old children with ASD (Gadow et al., 2004), the *hyperactive-impulsive* factor of DSM-IV defined ADHD loaded poorly on the ADHD syndrome (Gadow, DeVincent, & Pomeroy, 2006; Lecavalier et al., 2011). Poor loading of this factor may be due to underreport of the verbal hyperactivity-impulsivity items in young children with ASD (Lecavalier et al., 2011), but alternatively may indicate that ADHD *inattention* is more strongly associated with ASD (Lecavalier et al., 2011), and with social and language impairment (Gadow et al., 2006). Similarly, in a newly diagnosed sample of children with ASD aged 2-4 years, the highest scores among ADHD traits were found on attention problems and the underlying structure of this ASD phenotype that included co-occurring problems, consisted of two factors: a *Behavior-Repetitive Problem* and a *Social Communicative Deficit* factor on which both the Withdrawn and Attention scales loaded relatively high (Georgiades et al., 2011). These findings suggest a phenotypic overlap between attention problems and the core domains of ASD, rather than co-morbidity between distinct conditions.

3.2. Co-occurrence of ASD and ADHD symptoms or traits

Co-occurrence of ADHD symptoms in ASD

Clinical studies have investigated ADHD symptoms or traits in samples of young children with ASD by means of parent questionnaires. About 38% of children with an Autistic Disorder (AD) aged 1.5-5.8 years (Hartley, Sikora, & McCoy, 2008), and 17% of children with AD and pervasive developmental disorder (PDD-NOS) aged 2.5-5 years (Snow & Lecavalier, 2011) had clinical scores for attention problems on the Child Behavior Checklist (CBCL 1 ½ -5; Achenbach & Rescorla, 2000). Using the *Baby and Infant Screen for Children with autism traits-part 2 (BISCUIT-part 2) (Matson, Fodstad, & Mahan, 2009)* others have looked for co-occurring ADHD behaviors in ASD among children aged about 1-3.2 years from an early intervention sample of children with developmental delays (DD) including ASD (Fodstad, Rojahn, & Matson, 2010; Horovitz & Matson, 2013; Matson, Fodstad, Mahan, & Sevin, 2009; Matson, Hess, & Boisjoli, 2010; Matson, Neal, Fodstad, & Hess, 2010; Tureck, Matson, May, & Turygin, 2013). Moderate to severe problems in the composite domain of *inattention-impulsivity* and *tantrum-conduct behavior* (containing 6 items corresponding to the DSM-IV hyperactivity and impulsivity domains) were present in more than 50% of the ASD group (Matson, Fodstad, & Mahan, 2009). *Inattention-impulsivity* and *tantrum-conduct behavior* were more frequent and severe in the ASD than in the non-ASD delayed subgroup with effect sizes of .59 (p<.001) and of .14 (p<.001) respectively (Fodstad et al., 2010), and were associated with autism severity (Matson, Mahan, Hess, & Fodstad, 2010; Tureck, Matson, Cervantes, & Turygin, 2015). The strongest association was for co-occurring *Concentration Problems*, suggesting a more specific link of ASD with problems in attention. However, there was no effect of autism severity on rates of attention/ADHD problems in a sample of children with AD aged 1.5-5.8 years (Hartley et al., 2008), and in another 2.5-5 year old sample of children with ASD (Snow & Lecavalier, 2011). Here, absence of effect of autism severity may be explained by the highly homogeneous composition, i.e., low variance of autism severity, of the last two samples (Hartley et al., 2008; Snow & Lecavalier, 2011).

Similarly as for ASD and ADHD diagnoses, age effects were found on the co-occurrence of ASD and ADHD *traits*. Analyses by age group in an early intervention sample including children with ASD,

indicated lower rates and severity of co-morbid inattention-impulsivity problems in the younger subgroups aged about 1-2 years, compared to the older subgroups aged between 2-3.2 years (Fodstad et al., 2010; Horovitz & Matson, 2013). Age differences were not found in those with non-ASD related atypical development who, from the youngest age group, showed fewer co-morbid problems. This may indicate that ASD and ADHD behaviors reinforce each other and/or alternatively, that risks for ASD and for ADHD are linked. An age-related increase in observed ADHD behaviors was also found a large multisite ASD sample where parents reported significantly less ADHD symptoms (measured with the DSM oriented ADH CBCL-problem scale, but not when measured with the more concise attention problem CBCL-syndrome scale) in preschoolers aged 2.5-5 years than in school aged children and adolescents (Sikora, Vora, Coury, & Rosenberg, 2012). Variations in frequency of ADHD problems across studies might further be explained by differences between questionnaires, i.e. those with a narrow versus broad focus on ADHD and related behaviors, and by differences in the composition of the samples, i.e., AD, ASD, and ASD with DD.

Variations in co-occurring ADHD problems in children with ASD might also be related to IQ. This hypothesis warrants consideration because IQ, to a greater extent than autism severity, may contribute to high levels of inattention and impulsivity, a finding reported in adolescents with ASD (Simonoff et al., 2013). Also in 1.5-5.8 years old children with AD, non-verbal cognitive ability and low expressive language were the strongest predictors of symptoms of inattention and impulsivity in 1.5-5.8 years old children with AD (Hartley et al., 2008). Overall developmental quotient (DQ) had no significant effect on co-occurring problems when severity of autism was controlled for in two studies based on an younger early intervention sample of about 1-3.3 year olds with DD including ASD, although children in the low DQ category scored significantly higher on these problems (Fodstad et al., 2010; Matson, Mahan, et al., 2010). Of note, DQ included a broad range of developmental skills partly overlapping with ASD impairments and assessed via a parent questionnaire in the latter two studies, which cannot be equated to IQ. In sum, the findings suggest that ADHD problems increase with (preschool) age and are most prevalent in children with more severe ASD and lower IQ.

Co-occurrence of ASD symptoms in ADHD

Less is known about the reverse issue, the co-occurrence of core autistic symptoms or traits in young children with ADHD. It appears less common in ADHD research in preschoolers to report on co-occurring ASD symptoms. For example, in a study of children with ADHD nearly 25% presented with communication problems and ADHD severity was modestly associated with the CBCL 1 ½ -5 *Withdrawn domain* (r= 0.30, p< 0.001) (K. Posner et al., 2007), but a possible link of these problems with ASD was not tested. Nevertheless, several studies with preschoolers did examine global social functioning in ADHD and found lower social competence and more social problems (effect sizes >1.0) in both a clinical sample of 3 to 5 years old children with ADHD (DuPaul, McGoey, Eckert, & VanBrakle, 2001) and in two population based samples of about 4 year old children scoring high on ADHD symptoms (Julvez, Forns, Ribas-Fito, Torrent, & Sunyer, 2011; Thorell & Rydell, 2008). In the latter study the social difficulties consisted of low *pro-social orientation* (i.e. ability to engage in positive peer interactions) but not low *social initiative* (i.e. ability to initiate and take part in social interactions), possibly because poor social initiative is more related to internalizing problems, whereas increased social initiative may also reflect inhibition difficulties that often go with ADHD (Thorell & Rydell, 2008). In conclusion, aforementioned results are mainly indicative of increased occurrence of global (social) adaptive problems in relation to ADHD symptomatology, which problems also occur in the context of a broad range of other conditions.

Co-occurrence of ASD and ADHD traits in population samples

Because similar etiologic factors seem to operate along the continuum of severity of ASD and/or ADHD, it is crucial to also examine subclinical traits of ASD and ADHD and their associations in young population samples. To our knowledge, there is only one population based study that looked at the associations between ADHD behaviors and ASD traits at an early age: in a sample of 2 year old twins lower associations between ASD traits and ADHD behaviors based on DSM oriented scales of the CBCL 1 ½-5 (r=.23-26) were found than has been reported in older ages (r=.54-.57 and 0.72, respectively) (Ronald, Edelson, Asherson, & Saudino, 2010); moreover, the extent to which genetic influences were shared between the ASD and ADHD scales was modest (genetic correlation estimate of r=.27) (Ronald, Edelson,

et al., 2010), which is also less than reported in older children (r=.54-.57) (Ronald, Simonoff, Kuntsi, Asherson, & Plomin, 2008). These age related discrepancies may partly be explained by the less reliable measurement of ASD and ADHD behaviors in 2 years old children, as it is likely that many target behaviors might not yet be discernable at this age. Furthermore, the relatively low phenotypic and genetic correlations may also be due to the aggregation of ADHD domains into one factor, a method that ignores eventual domain specific associations.

3.3. Summary

The co-occurrence of ADHD diagnoses in young children at high risk for ASD and/or with ASD varies widely from less than 5% up to 40%. Co-occurrence rates were higher in children aged 3-6 years than in younger children (about 2.1 years of age), higher for inattention problems than for hyperactivity-impulsivity (but note that ratings of hyperactivity-impulsivity, particularly the verbal items, might be less reliable at young age), higher in clinical compared to population samples, higher in children with lower IQs than higher IQs and higher in studies that have used less stringent criteria for ADHD. Research on the co-occurrence of ASD- and ADHD traits indicates that between 17% and 50% of children with ASD show moderate to severe/clinical range ADHD-related behaviors and that these behaviors increase with age and autism severity, in line with findings on co-occurring diagnoses. The amount and severity of ADHD problems in children with ASD seem further related to lower IQ. The shared genetic influences on ASD and ADHD symptoms were also moderated by age such that the genetic correlation estimate was weaker in children aged 2 years in comparison to older children. In addition, the data show that among ADHD domains attention problems are most strongly associated with ASD domains and increase with severity of ASD and to a lesser extent with lower IQ, (Tureck, Matson, Cervantes, et al., 2015). Such concurs with results based on DSM-oriented ADHD criteria that show stronger associations between ADHD-inattention and social- and language/communication deficits (Gadow et al., 2006; Lecavalier et al., 2011). Associations between ASD and hyperactivity-impulsivity were weaker, but ratings of hyperactivity-impulsivity might be less reliable at young age. This would accord with the age-related increase in hyperactivity-impulsivity

scores in ASD during preschool years and also with the lack of associations between observed activity at 1 year and later ADHD (P. Johnson et al., 2014). The few studies in preschoolers with ADHD on social and communicative competence lack the necessary specificity to allow drawing any conclusions on core autistic symptoms in ADHD. The presentation of ADHD behaviors in ASD is more specific, but the data still raise questions about the similarity in constructs of ADHD behaviors in ASD versus ADHD. We will return to these questions in the discussion.

4. Temperament

Temperament traits can be defined as constitutionally based individual differences in the domains of activity, affectivity, attention, and self-regulation that are the product of interactions among genetic, biological, and environmental factors across time (Shiner et al., 2012) and that can be linked to neurobiological systems (Karalunas, Geurts, Konrad, Bender, & Nigg, 2014; M. I. Posner, Rothbart, Sheese, & Voelker, 2012; Rothbart, Sheese, Rueda, & Posner, 2011). The traits emerge early during development, are relatively stable and show a normal distribution in the population. Theoretically, temperament traits may be represented along a spectrum with ASD and/or ADHD, or as characteristics able to modify the presentation and outcome of ASD and/or ADHD. In accordance with a spectrum or common cause model temperament represents the subclinical manifestation of psychopathology and reflect a similar underlying structure as normal range behavior (Nigg, 2006). From this viewpoint temperament traits during early development may reflect increased risk for psychopathology or -at the extreme- may be identical to psychopathology (Egger & Angold, 2006). According to the vulnerability/moderator of outcome model, temperament traits contribute to the heterogeneity in presentation and outcome of psychopathology (Nigg et al., 2004). Although the two models imply strong concurrent associations between temperament and psychopathology, the vulnerability model also implies that temperament moderates the course of psychopathology (Martel, Gremillion, Roberts, Zastrow, & Tackett, 2014). Temperament can be framed in higher order patterns, that are composed of a diversity of more refined sub-traits that may be indexed at the behavioral, emotional, neural, physiological and/or genetic level (Nigg, 2006). Most temperament

frameworks converge on the prominence of three basic traits (Martel, Gremillion, & Roberts, 2012; Nigg, 2006): *withdrawal/negative affect* referring to anger, sadness, and fear; *approach/surgency* referring to high positive emotions, engagement with the environment, high activity and impulsivity (and perceptual sensitivity in infants), and lastly *effortful control* (EC) referring to attentional focus/shifting/duration of orienting, inhibitory control and low-intensity pleasure. The forerunner of EC in infancy that differs conceptually from EC at older ages is labelled *orienting/regulation* and includes soothability (speed of recovery from distress) and cuddliness (desire for warmth and closeness with others/enjoyment in and moulding of the body to caregiver) (Gartstein & Rothbart, 2003). This temperament EC/regulation domain is related to early emerging executive function (Jones et al., 2014; Rothbart, Ellis, Rueda, & Posner, 2003; Rothbart et al., 2011).

4.1. Temperament in ASD

Approach/surgency in ASD

Approach/surgency, either as composite temperament trait or as its components approach, activity and positive affect/mood, has been examined in seven studies conducted in infancy and preschool ages in relation to current or later ASD diagnosis or traits (Table 2.). As expected in ASD, low *approach/positive anticipation* is a consistent finding from 2 years onward: in an ASD group aged 3-7 years compared to a development delay and typical control group (Brock et al., 2012), in 2 and 3 years old HR siblings with a later ASD (HR-ASD) in comparison to HR siblings without later ASD (HR non-ASD) (Del Rosario, Gillespie-Lynch, Johnson, Sigman, & Hutman, 2014), and in a 2 years old HR-ASD group in comparison to a low risk group (Zwaigenbaum et al., 2005). A low *Behavioral Approach* profile, representing low positive anticipation, low attentional shifting and high level of non-goal-oriented activity, characterized a 2 year old HR-ASD group; of note, the HR non-ASD siblings who do not develop ASD and who also represent the broad autism spectrum (BAP), was rated as higher on *Behavioral Approach* than the HR-ASD and even low risk control groups (Garon et al., 2009), which may suggest that this high approach profile has a protective effect in the HR siblings. High levels of shyness (i.e., inhibition of approach in situations

involving novelty) were associated with social impairments on the Social Responsiveness Scale (SRS; Constanthino, 2002) in a 3 years old population sample (Salley, Miller, & Bell, 2013). Striking is that in the first year on the contrary, higher approach was generally found: in 6 months old HR-ASD versus HR non-ASD siblings; of note, this approach factor referred to both social and non-social stimuli and is thought to represent low inhibition rather than high social interest (Del Rosario et al., 2014). Similarly, higher surgency was reported at 7 months but no longer at 2 and 3 years of age in a HR-ASD group versus a HR non-ASD group; here, surgency rates were probably driven by high perceptual sensitivity at 7 months, an item included in surgency during infancy (Clifford et al., 2013; Gartstein & Rothbart, 2003).

For *activity*, the pattern also changed around the second year: first, decreased activity levels were reported in three studies at 6 months (and 1 year) of age in children with later ASD traits (Bolton, Golding, Emond, & Steer, 2012), and in HR-ASD in comparison to HR non-ASD siblings and low risk controls (Del Rosario et al., 2014; Zwaigenbaum et al., 2005). From the age of 2 years however, activity levels were no longer decreased in those with ASD (traits) and even reversed in the Bolton (2012) study where high activity levels at 2 years predicted autistic traits. Similarly, activity (without goal) was higher in 2 years old HR-ASD versus HR non-ASD and low risk groups (Garon et al., 2009), and in older preschool children with ASD (Brock et al., 2012). In contrast, low activity and low impulsivity (i.e. speed of response initiation) at age 3 and 4 years were associated with higher impairment on the SRS in a population sample (Salley et al., 2013). In the latter study low activity also referred to passivity/low reactivity to the environment, which may explain the discrepant findings.

Positive affect finally, included in the surgency/approach dimension was decreased in HR-ASD in comparison to HR non-ASD and low risk children at 1 year (Zwaigenbaum et al., 2005), and in comparison to low risk children at 2 years in HR versus low risk groups (Clifford et al., 2013; Garon et al., 2009). This is in accordance with reduced frequency and duration of smiling that has been demonstrated in 1 and 1.5 year old HR-ASD siblings (Filliter et al., 2014) and in accordance with reduced soothability and high discomfort in older children (Konstantareas & Stewart, 2006).

Negative affect in ASD

In six out of eight studies in ASD looking at temperament *negative affect* this trait was associated with autism. High levels of negative mood predicted autistic *traits* at 6 months and 2 years in a large population sample (Bolton et al., 2012); and high negative affect respectively low positive affect differentiated a HR 2 years old group with later ASD from a HR non-ASD outcome and low risk group (Clifford et al., 2013; Garon et al., 2009). Likewise, intense distress reactions, a component of negative affect, distinguished a HR-ASD from a HR non-ASD group at 1 year (Zwaigenbaum et al., 2005). A mixed temperament profile characterised by irritability, intolerance of intrusion, regulatory difficulties and including proneness to distress/ negative affect, was found in a case study with 9 HR infants who later developed ASD; in 3 of them these temperamental difficulties were already present at 6 months and became more evident with the later emergence of ASD symptoms (Bryson et al., 2007). Similarly, in a population sample discomfort (i.e., negative affect related to sensory qualities of stimulation) at age 2 years accounted for nearly 60% of the variance in social responsiveness, and higher fear level at age 3 years and sadness level at 4 years, were associated with stronger impairment on the SRS (Salley et al., 2013). Others did not find differences in negative affect/mood in HR-ASD compared to HR non-ASD at ages 6 months, 2 and 3 years (Del Rosario et al., 2014) and in a 3-7 years old sample with ASD (Brock et al., 2012). Of note, smaller between-group differences are expected when HR-ASD siblings are compared with HR non-ASD siblings as in (Del Rosario et al., 2014) instead of comparison with typical controls as in the other studies. Further, the latter two studies used the Carey Temperament Scales (CTS) based on the Thomas and Chess approach of temperament, that differs from scales based on related but distinct theoretical approach of Rothbart and colleagues used in the other studies (i.e., the Infant-/Early Childhood Behavior Questionnaires; IBQ/ECBQ). The latter scales have been reported to show greater stability over time and more stable internal consistency (Del Rosario et al., 2014).

Effortful control in ASD

Among the seven studies in ASD on effortful control (EC) and its infant counterpart orienting/ regulation six did find impairments in relation to ASD. Lower EC differentiated the HR-ASD from the HR non-ASD and low risk groups at 1.2 year and at 2 years of age, an effect that was accounted for by low cuddliness at this age (Clifford et al., 2013). By age 2 years, lower levels of *low intensity pleasure*, referring to quiet (social) activities, further differentiated this HR-ASD group from the other groups (Clifford et al., 2013). High *persistence* and low *distractibility* at 6 months of age predicted ASD *traits*, and high persistence at 2 years also predicted ASD *diagnosis* (Bolton et al., 2012). Similarly, low distractibility distinguished an ASD group from a typical- and developmental delayed group at age 3-7 years, and was associated with sensory hypo-responsiveness (Brock et al., 2012). Others who compared a HR-ASD group with a HR non-ASD group found overlapping rates of distractibility and persistence (6 measurements between the ages of 6 months and 3 years) (Del Rosario et al., 2014), suggesting that HR children who will not develop ASD are similar in these domains to those who will develop ASD. In the domain of shifting, low *disengagement of attention* at 1 year of age (Zwaigenbaum et al., 2005) and low *shifting of attention* at 2 years (Garon et al., 2009) differentiated the HR-ASD group from the HR non-ASD and low risk control groups. In the latter study low score on a composite *Effortful Emotion Regulation* profile (representing effortful attention and emotion control) further distinguished the whole HR group from controls, whereas low attentional focus distinguished the HR group without later ASD from the other groups (Garon et al., 2009). Also at age 4 years, low attention shifting was associated with social-communicative impairments on the SRS in a population sample (Salley et al., 2013). The three studies reporting on *inhibitory control* have found impairments: by age 2 year in a HR-ASD group (Zwaigenbaum et al., 2005) and in HR versus low risk children (Clifford et al., 2013), and by age 4 years in a population sample where low inhibitory control was associated with social-communicative impairments on SRS (Salley et al., 2013). These findings suggest that poor inhibition is a common feature of ASD and ADHD, although the data lack specificity to draw definite conclusions. We return on this issue when we discuss the cognitive data.

4.2. Temperament in ADHD

Approach/surgency in ADHD

In ADHD, high levels of approach/surgency is a consistent finding in the five studies conducted with infants and/or preschoolers (Table 2.). In the youngest sample, with 7 months old boys at familial risk for ADHD (fathers scoring high on ADHD symptoms, but ADHD status of child unknown) high activity level among other traits differentiated the HR from the comparison group (Auerbach, Atzaba-Poria, Berger, & Landau, 2004), and continued to differentiate the groups at 1 and 2.1 years (Auerbach et al., 2008). Surgency was positively correlated with hyperactivity-impulsivity and with inattention in 3-6 year old children high on ADHD symptoms (Martel et al., 2012; Martel et al., 2014), and in 3-5 years old children over-recruited for ADHD symptoms (Miller, Miller, Healey, Marshall, & Halperin, 2013). However, the association of surgency with inattention was less strong and even negative associations appeared when covariance between disruptive behavior symptoms, i.e., ADHD and Oppositional Defiant Disorder (ODD) symptoms, was controlled for (Martel et al., 2012). In the same line, surgency did not predict ADHD symptoms (Martel et al., 2014) and a factor derived from surgency that comprised impulsivity and high intensity pleasure, predicted hyperactivity but not inattention at one year follow up (Miller et al., 2013). These findings suggest that the low predictive power of surgency for ADHD symptoms was largely accounted for by the concurrent associations with ADHD symptoms, and that these associations were weaker with inattention.

Negative affect in ADHD

The five studies looking at *negative affect/emotionality* in relation to ADHD have consistently found high levels on this trait, both in infancy and at preschool age. In 7 months old boys at low versus high familial risk for ADHD (fathers scoring high on ADHD symptoms; diagnostic status child unknown), higher anger reactivity differentiated the HR from the low risk group; notably, this only applied to undirected anger, in contrast to directed anger which supposes a cognitive component involving a form of control (Auerbach et al., 2004). High rates of anger still differentiated the HR boys at 1 and 2.1 years

(Auerbach et al., 2008). In three other studies with preschoolers over-recruited for ADHD at 3-6 years, respectively 3-4 years of age higher scores on the composite negative emotionality scale were associated with all ADHD domains (Martel et al., 2012; Martel et al., 2014), and with severity of ADHD symptoms (Healey, Marks, & Halperin, 2011). When covariance between traits was accounted for, negative emotionality was differentially associated with hyperactivity-impulsivity but not with inattention (Martel et al., 2012), and did not predict one-year change in either ADHD domain (Martel et al., 2014). The low predictive power of negative emotionality and weaker associations with inattention than with hyperactivity is in line with the findings for surgency.

Effortful control in ADHD

The seven studies reporting on EC in relation to ADHD have all found impairments in overall EC or its components. In the youngest sample, children at familial risk for ADHD (ADHD scores of their fathers; ADHD status of child unknown) demonstrated lower levels of interest, i.e. shorter duration of orienting to- and manipulation of objects at 7 months, and lower levels of *purposefully* shifting of attention at 7 months and 1 year of age (Auerbach et al., 2004; Auerbach et al., 2008). At 2.1 years these difficulties also included weak focusing and sustaining of attention (Auerbach et al., 2008). Five studies have examined the associations of EC with ADHD symptoms in the child. It was found that lower *inhibitory control* was associated with ADHD- and behavior problems in a population sample of 2 year olds (Gagne, Saudino, & Asherson, 2011) and in a population sample of 3 year olds where low inhibition was the only observed temperament trait associated with ADHD (based on an extensive interview) (Dougherty et al., 2011). On a composite EC factor high scores were associated with all ADHD domains in children over recruited for ADHD (age about 3-6 years) (Martel et al., 2012; Miller et al., 2013), but see (Martel et al., 2014) where EC was only associated with hyperactivity-impulsivity. Further, EC did not predict one-year change of ADHD symptoms (Martel et al., 2014), suggesting that EC does not independently determine onset or course of ADHD during early childhood. Others found that high levels on the latent *cognitive control* factor, composed of temperament EC and executive function components, predicted fewer symptoms in all ADHD

domains at one year follow up, even when controlled for baseline levels of ADHD symptoms (Miller et al., 2013). This suggests that addition of executive function measures to EC increases the otherwise low predictive power of EC. In addition, EC and negative emotionality interacted such that low EC was associated with ADHD severity regardless of level of negative emotionality, but that in a context of high EC high negative emotionality too was associated with ADHD severity. This suggests that EC might be a primary pathway for ADHD and negative emotionality a secondary pathway (Martel et al., 2012).

Temperament and genetic factors in ADHD

The contribution of genetic factors on the temperament-psychopathology associations has been examined in two studies in ADHD with no equivalent in ASD. In one study, regulatory problems as temperament based measure at 3 months of age, combined with genetic risk (defined as the presence of the dopamine D4 receptor-7 repeat allele) increased the risk for ADHD at 11 years of age (Becker et al., 2010); neither regulatory problems nor genetic risk independently produced this effect. Of note, the regulatory problems comprised a broad range of behaviors (i.e., irritability including dysphoric, irritable and hypersensitive behavior, and hypo-activity including apathetic and hypo-reactive behavior) that are related to items falling under the surgency and negative affect domains in the Infant Behavior Questionnaire (IBQ) (Rothbart, 1981; Gartstein & Rothbart, 2003), and also comprised sleeping- and eating problems. Focusing on inhibitory control, others found that the variance in inhibitory control and ADHD symptoms in 2 years old twins was explained by common genetic influences and, to a lesser extent, by non-shared environmental influences (Gagne et al., 2011).

4.3. Summary temperament in ASD and ADHD

On *Approach/surgency*, high levels have been consistently found in HR-ASD siblings in the first year, followed by low levels from the age of 2 years, although HR non-ASD siblings showed a high behavioral approach profile at 2 years (Garon et al., 2009). Examination at item level indicates that high approach in the first year was mostly accounted for by increased non-social interests, perceptual sensitivity

and/or low inhibition instead of social approach. For activity, the reverse pattern was found, such that high (non-goal directed) activity levels were found from age 2 years in HR-ASD siblings or children high in autistic traits (but see Salley et al. 2013, where low activity at 3-4 years referred to passivity), preceded by low activity in the first year. In relation to ADHD, high surgency was consistently found: in the first through second year it was associated with familial risk for ADHD, and from 3 years of age with ADHD symptoms, although to a lesser extent with inattention.

High *negative affect/emotionality* was a consistent finding in relation to both ASD and ADHD. From around 6 months of age, increased negative mood, at 1 year increased distress reactions, and from 2 years discomfort related to quality of sensory stimuli, shyness, sadness and fear are reported in those children with a later ASD or with ASD traits. In ADHD, in the first through second year high anger reactivity, specifically undirected anger, is associated with familial risk for ADHD. At age 3-5 years, associations between high scores on the composite negative affect trait and ADHD symptoms is a consistent finding. Thus, although high negative affect is a shared characteristic of ASD and ADHD, there is some dissociation in the content of this trait in ASD versus ADHD. In ASD, distress, shyness, fear and sadness seem to prevail whereas in ADHD anger prevails, which may suggest that negative affect points to different underlying mechanisms in ASD versus ADHD.

In both ASD and ADHD, deficits in effortful control (EC) are consistently found. In ASD, EC problems like low distractibility, high persistence and low disengagement and shifting of attention are already reported in the first 2 years of age (except for HR-ASD siblings who also tended to score lower on attentional focus at 2 years in Garon et al.,2009), and problems with inhibitory control by the age of 2 years. In relation to ADHD, findings suggest that already in the first year low EC can be observed in children at familial risk for ADHD, reflected as low persistence/high distractibility and as low purposefully shifting of attention that are followed by low attentional- and inhibitory control from the age of 2 years. From age 3-6 years, overall low EC and specifically low inhibition is associated with ADHD symptoms. Temperament at this age did not independently predict ADHD course, but EC predicted ADHD when combined with executive functioning.

5. Executive function

Cognition is a general term for the mental processes involved in gaining meaning and knowledge from information and selecting appropriate responses in order to adapt flexibly to the ever changing environments. Both higher-order and more basic functions are involved in cognition with largely known neuronal underpinnings that are etiologically linked to- and may alter- development, such as information processing and executive function (EF) (Johnson, 2012; Keehn, Muller, & Townsend, 2013; Russo et al., 2007; Sonuga-Barke, Sergeant, Nigg, & Willcutt, 2008). Given the broad range of processes involved in EF, not surprisingly both ASD and ADHD are associated with cognitive dysfunctions. Nevertheless, research indicates that large variations exist in type and severity of dysfunctions between affected individuals (Charman et al., 2011; H. Geurts, Sinzig, Booth, & Happe, 2014; Hill, 2004; Johnson, 2012; Nigg, Willcutt, Doyle, & Sonuga-Barke, 2005; Rommelse et al., 2011) and that EF is only moderately predictive of the core symptom domains (Johnson, 2012). In this light, EF involves processes that cut across disorders and that may help understanding the unique and shared characteristics of ASD and ADHD. As research on EF in in young children with ASD or ASD traits is limited in contrast to ADHD, we also briefly refer to temperament effortful control findings in ASD in this paragraph.

Executive function

Executive function (EF) is an umbrella term for neuropsychological functions that involves the domains of working memory, inhibition and cognitive flexibility (shifting). Research on EF in ASD and in ADHD has mostly used these domains and a few studies have used composite EF domains (Appendix. Table 2.)

5.1. Executive function in ASD.

Two of the four studies looking at *composite EF domains* in relation to ASD, have found no impairments in comparison to typical children and children with developmental delay at 2.9 years (Yerys, Hepburn, Pennington, & Rogers, 2007) and at 3-4 years of age relative to typically developing children

matched on mental age (Dawson et al., 2002). The other two studies have found impairments in all EF domains at the ages of 4.4 years (Smithson et al., 2013) and 5-7 years (Rosenthal et al., 2013). These discrepancies probably come from differences between studies in age of the samples and in method of measurement. At the younger age of the Dawson et al. (2002) and Yerys et al. (2007) samples, current neuropsychological tests might not be sensitive enough to detect EF dysfunctions. Alternatively, EF undergo substantial developmental changes in early childhood and may then be poorly differentiable from normative variations in maturation of these functions (Pauli-Pott & Becker, 2015). Another explanation for the discrepancies is the type of comparison group. In Dawson et al. (2002) the ASD group was compared to a MA-matched delayed group and a MA-matched group which included children who were probably too young for the tests (1-3.8 years versus 3-4 years in the ASD group). However, another study in ASD using appropriate comparison groups i.e., a developmental delay group matched on both CA and overall MA, and a CA-matched group (Yerys et al., 2007) also failed to detect EF deficits in ASD relative to both comparison groups. Of note, this sample was still younger (mean age 2.9 years) than the ASD sample of Dawson et al. (2002), which calls into question the developmental appropriateness of the EF tests. This may also explain why EF impairments were found in the two studies that used a questionnaire (BRIEF; (Gioia, Isquith, Guy, & Kenworthy, 2000) measuring other EF aspects than neuropsychological test (Rosenthal et al., 2013; Smithson et al., 2013). Although EF were not associated with ASD status in Dawson et al (2002), several EF tasks were associated with joint attention performance, suggesting that EF are required for joint attention abilities. In the same line, EF (including planning, cognitive flexibility, and inhibitory control) in children with ASD aged 4-7 years predicted theory of mind (ToM) ability about three years later over and above the variance by age, cognitive ability, and children's initial ToM performance; the reverse did not apply i.e., there was no independent relationship between children's initial ToM skills and later EF (Pellicano, 2010), suggesting that EF develop primarily to ToM skills. This has been found in typical developing preschoolers as well (Muller, Liebermann-Finestone, Carpendale, Hammond, & Bibok, 2012).

Working memory in ASD

Working memory (WM) has been investigated in 6-9 months old infants siblings at risk for ASD using a peekaboo game that differentiated between social versus non-social targets. The HR-ASD siblings showed better WM for non-social targets (and same WM for social targets) in comparison to low risk siblings (Noland, Steven Reznick, Stone, Walden, & Sheridan, 2010). At older age, impaired WM (according to a parent questionnaire for EF) was found in a sample of children with ASD; in the sample that was split into four age groups between 5-7 years and 14-18 years, impairments were significantly higher in the older age groups even after controlling for IQ and ASD severity (Rosenthal et al., 2013).

Inhibition in ASD

To our knowledge, the only study on *inhibition* in young children has been conducted with high functioning children with ASD (mean age 4.9 years); no differences were found on a Stroop-like inhibition task but more impairments in *inhibitory self-control* on an EF questionnaire, relative to typically developing children (Jahromi, Bryce, & Swanson, 2013). Further, the composite EF inhibition score (inhibition task and inhibitory self-control on questionnaire) explained most variability in emotion regulation above and beyond other dimensions of self-regulation, and predicted emotional and school engagement. Because of the limited data on the EF domain of *inhibition* in young children with ASD (traits), and the relatedness between temperamental effortful control (EC) and EF (Nigg, 2006), we also briefly report on research using these related temperamental traits. In the above sample of children with high functioning ASD, temperamental EC emerged as potential protective factor for pro-social peer engagement in the ASD group only (Jahromi et al., 2013). Low temperamental *inhibitory control* was found in 2 years old HR siblings (Zwaigenbaum et al., 2005), specifically in HR-ASD siblings (Garon et al., 2009), and at age 4 years this trait was associated with concurrent impairments in social orientation and communication using the SRS (Salley et al., 2013). On the EC subscale *Attentional Focus/Duration of Orienting*, longer duration of orienting to objects at 6 months and 1 year of age, and reduced attentional shifting at 2 years of age were

found (Zwaigenbaum et al., 2005) as well as low distractibility and high persistence in HR siblings with a later ASD diagnosis (Bolton et al., 2012) and in 3-7 year olds with ASD (Brock et al., 2012).

Shifting/cognitive flexibility in ASD

The two studies that have tested shifting/cognitive flexibility in young children with ASD did find impairments on those traits. In a group of 5-7 years old children with ASD the largest impairments on a parent EF questionnaire were in the domain of cognitive flexibility; interestingly, impairments in shifting were equally high across all child and adolescent groups in contrast to other EF that became more pronounced with age (Rosenthal et al., 2013). Others found that lower performance on shifting (and planning) on neuropsychological tasks characterized a group with ASD in comparison to a group with typical development (mean age 4.9, respectively 4.6 years); in the ASD and control groups cognitive shifting and planning (and verbal IQ) contributed to better *Theory of Mind* (ToM) skills, suggesting that ToM is primarily mediated by cognitive abilities rather than by ASD symptoms (Kimhi, Shoam-Kugelmas, Agam Ben-Artzi, Ben-Moshe, & Bauminger-Zviely, 2014).

5.2. Executive function in ADHD

Research on early EF in ADHD has mainly been conducted in children of preschool age, with two meta-analyses covering this area. We will confine to the findings on EF in ADHD published after august 2011 in light of the conclusions in the meta-analyses. In the first meta-analysis in preschoolers at risk for ADHD (25 articles published up to 2009; n=3005 children; mean age between 3-6 years), the authors concluded that deficits in almost all basic cognitive domains, i.e., simple response suppression and interference control of response inhibition, interference control, delay aversion and vigilance-arousal, were associated with concurrent and later ADHD symptoms (Pauli-Pott & Becker, 2011). Comparable results on EF in ADHD were found in the second meta-analysis (22 articles published up to august 2011; n=4021 children; mean age between 3-6 years) (Schoemaker, Mulder, Dekovic, & Matthys, 2013).

Working memory in ADHD

Three out of the four recent studies on WM in relation to ADHD in young children have found weak associations with ADHD symptoms: in a population sample over recruited for ADHD (mean age 4.3 years) (Martel, Roberts, & Gremillion, 2013); and in two slightly younger population samples (mean age 3.5 years) (Rohrer-Baumgartner et al., 2014; Skogan et al., 2014) although in the latter study WM did not differ between the ADHD and typical control groups (Skogan et al., 2014). Similarly, in a clinical sample of children with ADHD (mean age 4.6 years) WM did not differ between the ADHD and ODD or typical control groups (Schoemaker et al., 2012). These recent findings are in line with conclusions from both meta-analyses that at very young age WM is at best only very weakly (effect size 0.17) associated with ADHD (Pauli-Pott & Becker, 2011; Schoemaker et al., 2013), which is in contrast to findings at older ages (Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005).

Inhibition in ADHD

Inhibition is probably the most examined EF in preschoolers (Garon, Bryson, & Smith, 2008), particularly in ADHD and disruptive behavior disorders. All five recent studies on inhibitory control (IC) in young children have found that IC impairments were associated with ADHD. This was found in two population samples over recruited for ADHD (mean age 4.3 and 3.5 years) (Martel et al., 2013; Rohrer-Baumgartner et al., 2014), and in a clinical sample with ADHD (mean age 4.6 years) (Schoemaker et al., 2012). The latter two studies did control for IQ, and Martel et al. (2013) and Shoemaker et al. (2012) also for co-morbid disruptive behavior problems. Regarding the specific effect of co-morbid problems on the EF-ADHD associations, reduced inhibition differentiated the “pure” ADHD- and ADHD group with oppositional defiant disorder (ODD) problems from the typical control group (mean age 3.5 years) (Skogan et al., 2014). Similarly, others found that IC was worst in the ADHD group with high co-morbidity (disruptive behavior and/or internalizing problems), whereas high delay aversion (DA) (i.e., reward related inhibitory control) was associated with pure ADHD regardless of comorbid problems (Pauli-Pott, Dalir, Mingebach, Roller, & Becker, 2014), suggesting that at young age DA is more specifically associated with

ADHD whereas IC is also associated with a broad range of other problems. However, the strength of this association might have been overestimated by the absence of co-morbid internalizing problems which generally go with low DA (Pauli-Pott et al., 2014). Nonetheless, the findings concur with those of the meta-analyses i.e., medium effect size for inhibition (Schoemaker et al., 2013), medium to large effect sizes for response inhibition and delay aversion, and slightly lower for vigilance/arousal and interference control (Pauli-Pott & Becker, 2011).

Age effects were also reported in the meta-analyses, such that the predictive values for ADHD decreased with age for DA tasks, and increasing with age for interference control and vigilance/ arousal tasks (Pauli-Pott & Becker, 2011). It is assumed that abilities on DA tasks (i.e. ability to suppress a motivational response) mature earlier (Garon et al., 2008) and can most specifically be assessed at younger preschool age before integration with other components takes place. This is in contrast to interference control tasks and vigilance/arousal which may still undergo substantial changes during the early preschool years (Pauli-Pott & Becker, 2011). Different age effects were reported in the other meta-analysis where associations of overall EF and inhibition with ADHD symptoms (and externalizing behavior problems) were stronger in the older (4 ½- 6 years) compared to the younger age group (3-4 ½ years) (Schoemaker et al., 2013). The discordant age effects may be partly explained by the broader target group (i.e., externalizing problems) in Schoemaker et al. (2013), and the different approach to age as a continuous variable (Pauli-Pott & Becker, 2011) versus categorical variable (Schoemaker et al., 2013).

Shifting/cognitive flexibility in ADHD

This is the least explored executive domain in relation to ADHD in young children, which showed the lowest effect size (0.13) (Schoemaker et al., 2013) compared to other EF domains (Pauli-Pott & Becker, 2011; Schoemaker et al., 2013). In the one recent study on shifting conducted in a population sample over recruited for ADHD (mean age 4.3 years), worse set shifting was associated with increased ADHD symptoms and inattention (Martel et al., 2013), suggesting that shifting deficits are also present in ADHD.

Interactions among executive function, effortful- and affective/motivational control in ADHD

The role of affective or motivational control in the EF-ADHD associations has been examined in three studies. One found that in the context of high negative emotionality strong neurocognitive functioning had no protective effect, in contrast to a context of less severe negative emotionality wherein strong neurocognitive functioning was a significant protective factor for ADHD severity in 3-4 years old children (mean age 4.3) (Healey et al., 2011). In the same line, others found that affective control (defined as control processes that occur more reflexively and that included one DA task), but not effortful control was concurrently associated with cognitive control (i.e., executive functions tasks) in ADHD in 4-6 years old children (mean age 4.3) (Martel et al., 2013). Further, temperamental anger/frustration at age 3-4 years had a negative impact on the development of EF at age 6 years, and predicted ADHD symptom severity at age 7 years together with EF at age 6 years independently from early EF (Rabinovitz, O'Neill, Rajendran, & Halperin, 2016). These findings suggest that affective forms of control might play an important role in the early development of ADHD, possibly as precursors or foundation of more cognitive forms of control (Healey et al., 2011; Martel et al., 2013).

Longitudinal associations between executive function and ADHD

Given the relatively strong associations between EF and ADHD and ASD, one may question how these associations arise and develop in parallel. Two studies have examined the longitudinal associations between EF/neuropsychological functioning and ADHD (and no study in ASD) in a sample of children recruited at 3-4 years of age and followed annually until their seventh-eighth year. Changes in EF/neuropsychological functioning, not baseline levels, were associated with the trajectory of ADHD symptoms and impairment, suggesting that early EF is not etiologically linked to the ADHD trajectory but acts as a moderator of outcome (Rajendran, Trampush, et al., 2013). Indeed, the magnitude of change in EF was linearly and inversely associated with the trajectory of ADHD severity and impairment (Rajendran, Trampush, et al., 2013). Improved EF only predicted the diminution of ADHD severity in the high ADHD group from age 4-5 years (Rajendran, Rindskopf, et al., 2013), which might indicate that children scoring

high on ADHD are more susceptible to the moderating effect of EF than typically developing children. Striking is that the direction of these associations changed over time as from age 5-6 years greater ADHD severity also predicted subsequent changes in EF even in those with modest ADHD scores, suggesting that from older preschool age the moderating effect of EF on ADHD severity becomes reciprocal (Rajendran, Rindskopf, et al., 2013).

5.3. Summary executive function in ASD and ADHD

The few studies on early EF in ASD suggest that deficits can be measured from 4 years of age, particularly when assessed with questionnaires instead of neuropsychological tests (but see in Kimhi et al., 2014). EF was associated with joint attention and with ToM and appeared to play a major role in later emotion regulation and behavioral school engagement (Jahromi et al., 2013). Findings in ASD further suggest that deficits in the domain of shifting are the most prominent at earlier age (5-7 years), and are relatively stable in comparison to the other EF deficits that increase with age. The far greater amount of studies in ADHD where EF have been measured from about 2.5 years of age, show that associations with ADHD are strongest for inhibition and weaker for WM, and tend to increase with age. Shifting has the smallest effect size but has scantly been tested in ADHD at young ages. It further seems that affective or motivational forms of control play a dominant role over EF in the early development of ADHD, suggesting that different regulating systems are involved in the early trajectories to ADHD, which may further partly account for the heterogeneity of ADHD (Nigg & Casey, 2005; Nigg et al., 2004; Sonuga-Barke & Halperin, 2010).

6. Discussion

With the present review of the literature on the core symptoms, temperament and cognition in relation to ASD and ADHD during infancy and preschool age, we identified unique and shared characteristics in the early trajectories of ASD and ADHD. In the following sections we discuss several theoretical implications and the challenges raised by the literature.

6.1. What may explain lower ASD-ADHD co-occurrence below the age of three?

The data clearly show that symptoms or traits of ASD and ADHD frequently co-occur, but that this co-occurrence is much lower in children below the age of 3 years. The lower co-occurrence of ASD and ADHD symptoms or traits at very young age may be an artefact due to measurement problems in the first 3 years of life. Alternatively, age differences may be explained in terms of possible trajectories of ASD-ADHD associations in that the two conditions are linked by common (genetic) risks but that overt symptoms emerge or express at different times. A third explanation is that ASD and ADHD are not strongly linked at the very beginning but characteristics of the two conditions interact and increasingly become intertwined over the course of development. Such cascade effects may further be moderated by additional risk or protective factors. These mechanisms may explain the lower genetic correlation between ASD and ADHD during the first years compared to older ages (Ronald, Edelson, et al., 2010). Cascade effects may also explain the larger increase of ADHD symptoms over time: 1) in children with ASD in contrast to those without ASD; 2) in children with ASD who had already relatively high ADHD scores in the first years (Fodstad et al., 2010; Horovitz & Matson, 2013); and 3) in those with lower IQ. Two longitudinal studies with older children showed that ADHD symptoms or traits were more strongly predictive of ASD traits than the reverse (St Pourcain et al., 2011; Taylor et al., 2012). Unfortunately, the mostly cross-sectional data in infants and toddlers hinders to disentangle the bidirectional effects of ASD on ADHD development and the effects of persistence and severity of early emerging ADHD symptoms on the course of ASD, but available data suggest that cascade-effects can certainly not be ruled out, emphasizing the need for early detection and intervention.

6.2. Attention problems as common pathway to ASD and ADHD

A consistent finding is that among ADHD (related) behaviors the factor inattention or attention problems is most strongly associated with ASD domains, a relation that could already be measured at age 1.5 years (Tureck, Matson, Cervantes, et al., 2015). This suggests that inattention overlaps with the ASD

core domains at the phenotypic level and may indicate that early inattention forms a common pathway to ASD and ADHD. This hypothesis concurs with findings in 7-15 years old twins that variation in internalizing/externalizing behaviors (on the CBCL) accounted for about 50% of variation in autistic traits (on the SRS), with most contribution coming from the Attention- and Social Problems scales (Constantino, Hudziak, & Todd, 2003). In the same line, preliminary findings in adults show that the co-occurrence of ADHD and ASD symptoms or traits is due to shared attention problems, specifically by problems in attentional switching, and that this association has a genetic basis (Polderman et al., 2013). However, a complicating factor is that it is unclear whether attention problems in ASD and in ADHD assessed by rating scales refer to or are based on the same underlying cognitive and neural mechanisms. For these attention scales also include items that fall outside the pure attention domain (*clumsy*, *shifts quickly*, *can't sit still*, *wanders away*). Furthermore, there is some entanglement of symptom descriptions between ADHD and ASD: the DSM-5 ADHD-inattention item "does not seem to listen when spoken to directly'' may indicate 1) direct inhibition problems and pure distractibility, or 2) specific problems with social attention, and/or 3) be due to sensory processing peculiarities and preoccupations that hamper the ability to attend to complex social cues. These latter two are clearly entangled with ASD. Further complicating the matter is that inattention is a multifaceted construct that can be operationalized in terms of disturbances in focusing, sustaining and/or shifting and disengagement of attention. For example, in adults with ASD traits or ADHD problems, attention shifting referred to 'the ability to easily switch attention', 'perform simultaneously multiple tasks' or 'follow multiple conversations', which imply the coordination of many different skills (Polderman et al., 2013). To elucidate the underlying unique and common mechanisms of inattention in ASD and in ADHD, it may therefore be helpful to model attentional functions in terms of partly separable but interacting networks with known neurobiological underpinnings such as the alerting, orienting and executive control networks according to the Posner model (Keehn et al., 2013; M. I. Posner & Petersen, 1990). It thus remains to be determined how problems in the development of these networks differentially relate to later emerging ADHD and ASD symptoms.

6.3. A motivational model to explain temperament differences between ASD and ADHD

High negative affect (referring to distress reactions, anger, fear and/or sadness) stands out as a shared temperamental characteristic of ASD and ADHD beginning in the first year. However, the differential traits of early negative affect in ASD (mainly distress, fear and sadness) versus ADHD (mainly anger) may be explained by motivational deficits, more precisely differences in approach and withdrawal (see review by Nigg, 2006).

In ASD, negative affect is associated with withdrawal but is preceded by approach (see Fig. 1). As the initial high approach/surgency in ASD seems mainly driven by high perceptual sensitivity, increased non-social interests and little control over orienting ("obligatory attention"), the reversing of approach into withdrawal after the first year may be explained as cascade-effects between these traits and ongoing sensory input. As a result, sensory overload may occur, leading to increased negative affect and ultimately withdrawal reactions. In young children with ASD, poor social motivation and low control of attention (low disengagement) may further hinder the effective regulation of distress by caregivers and development of more mature forms of control. Indeed, orienting to novelty, with the aid of the caregiver, has a regulatory function during infancy (Rothbart et al., 2011), and has been related to higher surgency/positive affect and lower negative affect in typical infants (Gartstein & Rothbart, 2003). Similarly, the reversing of temperamental activity in ASD from low into high scores during the first years may be understood not only a result of delayed locomotor development (Leonard et al., 2013) but as atypical or incongruent incentives and (social) motivation for activity. For example, high motor activity without goal at 2 years in HR-ASD children combined with low positive anticipation, suggests a dissociation between motivation, affect and activity (Garon et al., 2009). In ADHD, where research in infancy is limited, one may hypothesize that a combination of impulsive approach to novelty and excessive excitement and motivation for immediate (social) reward, may lead to dysregulation that is based on different mechanisms than in ASD. Taken together, a motivational perspective on negative affect and activity suggests that ASD and ADHD differ in these domains and provides a model for understanding these differences.

6.4. Low effortful control may have different underpinnings in ASD and ADHD

It may be hypothesized that low effortful control points to low social motivation and low disengagement in ASD, and to low sustained attention and high distractibility in ADHD. Low EC in ASD referred to low distractibility and disengagement and low levels of c*uddliness* and of *low intensity pleasure* (see Fig.1). The latter components of EC in infants stand for low affiliative behaviors and low pleasure derived from activities involving low intensity, complexity, novelty, and incongruity like many quiet social activities such as being sung to, being rocked, and listening to a story. In contrast, low EC in ADHD referred to low *interest* which stands for short duration of orienting attention to or interacting with an object (see Fig. 1). In other words, early in development low scores on the EC trait of *attentional shifting* in ASD and ADHD seem to represent *opposite* tendencies underlying reduced attentional control, with ADHD being associated with low levels of *intentional* shifting of attention, possibly as a consequence of quick and unintentional disengagement due to poor sustained attention/high distractibility, and ASD being associated with low attentional shifting/distractibility and low levels of social driven behaviors. In conclusion, seemingly similar behavioral characteristics may point to diverging and even opposite underlying mechanisms, emphasizing the need to look at behavioral correlates and contextual and motivational factors before interpreting individual characteristics.

6.5. What is measured with EF in ASD and ADHD?

There is a large variety between studies in the methods used to test EF, and consequently in the cognitive components being tested. It has been argued that children with ASD mainly fail on inhibition tasks when these are combined with other EF or when tasks require more complex cognitive abilities (Keehn et al., 2013). The same applies for tasks and contexts with high social demands (Kenworthy et al., 2008). Children with ASD may also have more difficulties with tasks that are open-ended, lack explicit structure or involve arbitrary rules (White, Burgess, & Hill, 2009). Accordingly, low performance on such tasks in ASD should perhaps not primarily be assigned to executive dysfunction, but to ‘difficulties forming an implicit understanding of the experimenter’s expectations for the task’(White, 2013), an hypothesis that needs to be

tested. In this line, others did find that difficulties learning from social feedback rather than lexical principles limit vocabulary building in toddlers at risk for autism (Bedford et al., 2013). Regarding ADHD, procedures controlling for non-inhibitory and non-attentional EF components in preschoolers resulted in no clear ADHD-related executive dysfunction, suggesting that at young age EF is rather intact and that lower performance on EF tasks may be attributed to behavioral dysregulation or poor state regulation (Berwid et al., 2005; Marks et al., 2005). Moreover, along with the cognitive components of EF, affective or motivational components involved in choice delay tasks should be taken into account as these seem differentially related to the core symptoms (Castellanos, Sonuga-Barke, Milham, & Tannock, 2006) and play a major role in the early pathways to ADHD. This concurs with the common genetic effects contributing to the association between emotion regulation and working memory (Wang & Saudino, 2013). The literature thus suggests that EF impairments in ASD and ADHD in young children may partly be attributed to (social) information processing, motivational or regulatory processes that are difficult to isolate within complex EF tasks.

6.6. What can explain age related increase in executive function problems in ASD and ADHD?

The detection of EF problems in young children largely depends on age at assessment and type of EF measures (Garon et al., 2008; Kenworthy, Yerys, Anthony, & Wallace, 2008; Pauli-Pott & Becker, 2015). In ASD, the reviewed data suggest that only from 4 years of age and for most on a questionnaire, EF impairments can be detected relative to control groups (but see Kimhi et al., 2014). The substantial developmental changes in EF during the first years of life may hinder the reliable distinction between deficits and normative variations in maturation of these complex functions (Garon et al., 2008; Pauli-Pott & Becker, 2015). However, using methods adapted for very young age, differences in *components* of EF (e.g. better working memory for non-social targets relative to controls) have been detected in HR-ASD infants relative to controls. Moreover, HR-ASD infants have shown atypicalities on basic temperament EC traits related to EF (e.g., longer duration of orienting, low visual disengagement and low attentional shifting), and on visual attention tasks (Falck-Ytter, Bolte, & Gredeback, 2013; Guillon, Hadjikhani,

Baduel, & Roge, 2014). The above suggests that precursors and basic *components* of EF are already in place and may show atypicalities in infants with later ASD, in contrast to complex EF domains which follow prolonged developmental trajectories. A different and less pronounced age effect on EF appears in ADHD, where deficits in most EF domains have been found from about 2.5 years and which increase during preschool age. Further, the domain-specific age effects in ADHD point to dissimilarities in maturational course between EF domains (Garon et al., 2008; Pauli-Pott & Becker, 2011). Specifically, deficits in delay aversion and inhibitory control could be detected earlier than those in working memory and in shifting, which is in contrast to ASD where deficits in shifting were the first to appear. Based on the few studies on EF in young children with ASD versus ADHD it may tentatively be concluded that maturation contributes to the later appearance of deficits in complex EF during later preschool age in children with ASD. The earlier appearance of EF deficits in ADHD further points to different processes involved in the early development of EF in ADHD versus ASD, which is also supported by the different sequence in which EF deficits appear.

6.7. Executive function in the pathways to ASD and ADHD

The absence of clear EF deficits in children with ASD below the age of about 4 years relative to MA and CA matched children, suggests that EF deficits are not primary deficits in ASD (Yerys et al., 2007). EF may rather be a non-specific risk- or protective factor (Johnson, 2012). For example, EF independently predicted ToM in 4-7 years old children with ASD (Pellicano, 2010). In ADHD, change in EF but not baseline levels predicted ADHD trajectories in preschoolers (Rajendran, Trampush et al., 2013). This moderating effect of EF on ADHD severity became reciprocal from older preschool age (Rajendran, Rindskopf et al., 2013), suggesting that over time EF is increasingly influenced by functions in other brain systems (Johnson, 2012). Furthermore, the literature in ADHD points to different and dissociable neuropsychological pathways to ADHD (Castellanos et al., 2006; Sonuga-Barke et al., 2008). Two important pathways are the more cognitive EF required for abstract or decontextualized problems, in contrast to the affective or motivational EF required for problems with high affective value (Castellanos et

al., 2006). It seems that during preschool age, motivational processes as measured in response inhibition tasks (DA) and negative affect play a relatively important role in EF in relation to ADHD. DA and IC at this age also mediated the link between familial risk, not prenatal and psychosocial risks, and ADHD symptoms, stressing the role of DA and IC in the pathways to ADHD and suggesting that different neuropsychological pathways are related to familial versus prenatal/psychosocial risks (Pauli-Pott, Dalir, Mingebach, Roller, & Becker, 2013).

The moderating role of complex EF in ASD and ADHD, may also apply to precursors or basic components of EF, e.g. attentional shifting and -control, and temperament effortful control, that have extensively been investigated in relation to ASD. Notably, research supports the idea that atypicalities in these precursors or basic functions in infancy may precede deficits in compound EF domains and core symptoms. This connectedness between basic functions and complex EF also suggests that brain regions involved in later EF are already supporting some EF precursors skills early in infancy (Johnson, 2012).

Taken together, compound EF domains show a moderating and partly mediating role in the pathways to ADHD and ASD during preschool age. Dysfunctions in precursors or basic components of EF in infancy may precede complex EF and behavioral symptoms, which possibly points to their causative role in the trajectories to ASD.

7. Challenges and recommendations for future research

In the next section we elaborate on limitations of the current literature for allowing conclusions about early unique and shared antecedents of ASD and ADHD, and provide recommendations for future research.

7.1. Difference in age range between ASD and ADHD research

The difference in age range between ASD and ADHD is an important obstacle when examining the links between the early trajectories of ASD and ADHD. Research in ASD has focused on the first three years of life with relatively few studies covering the preschool age whereas in ADHD the opposite is the

case. The younger start of conducting research in ASD, facilitated by the wide use of HR-designs, and age-appropriate assessment techniques beginning in infancy using well validated diagnostic instruments has not been equaled in ADHD. Although validated instruments have recently been developed that enable reliable assessments of ADHD symptoms from younger preschool age (Bunte, Laschen, et al., 2013; Bunte, Schoemaker, Hessen, van der Heijden, & Matthys, 2013; Keenan et al., 2007; Wakschlag et al., 2008), substantial diagnostic instability of ADHD is found from preschool- to early school age (Bunte, Schoemaker, Hessen, van der Heijden, & Matthys, 2014). To understand such heterogeneity of ADHD pathways and the possible links with ASD from the earliest stages, priority should be given to early precursors of ADHD before diagnostic outcomes are established (Sonuga-Barke & Halperin, 2010).

In addition, the normative changes in behaviors, temperament traits and cognitive functions during the first years need to be better understood before extrapolation to ASD and ADHD can take place. For example, one temperament trait may refer to different mechanisms across age periods, as demonstrated by the changing context and motivation for approach components from infancy to toddlerhood in relation to ASD. Changes in the behavioral correlates of temperament traits over time also reflect shifts in the underlying neurobiological mechanisms (Rothbart et al., 2011). This favors the use of temperamental models that can be linked to neurobiological mechanisms. For cognition, the complex and prolonged developmental trajectories of EF (see review (Kenworthy et al., 2008) imply that cognitive impairments should be followed over lengthy periods including at least preschool age. For example, infant (6, 12 months) and toddler (2, 3 years) abilities in the domains of visual attention, processing speed, and memory appear to predict EF at school age (Rose, Feldman, & Jankowski, 2012). Similarly, studies in typical infants and young children using behavioral methods to test basic executive components in combination with neuroimaging, reveal that some functions of the executive network (e.g. error detection) are already present in the first year, but that the ability to take action based on errors/conflicts is delayed until about 3-4 years of age. These changes correspond to maturational changes in brain functioning, like increase in connectivity between brain areas (M. I. Posner et al., 2012; Rothbart et al., 2011). To understand the early developmental trajectories of psychopathology, it is therefore crucial to investigate basic components of behavior and

cognition that are less dependent on immature functional skills and motivation along with more complex functions and adaptive skills as they develop over time.

7.2. Composite domains or factors versus subdomains and basic functions

In the literature widely diverging procedures have been applied to measure symptoms, temperament and cognition. These measures mostly result in scores on composite factors that may appear similar but often differ across studies and across ages at the more basic behavioral level. This impedes linkage with specific behavioral and functional components, and linkage with biological systems across developmental periods (Klin, Shultz, & Jones, 2014). For example, the social problems reported in ADHD mainly referred to non-specific social-adaptive and coping problems, and the correlates of hyperactivity and inattention also vary with age and diverge between ASD and ADHD. Further, several subdomains have been disregarded; restrictive-repetitive behaviors have not been tested separately in young children at high risk for ADHD or with ADHD. This is a shortcoming in view of the differential associations between subdomains found at older ages. Specifically, hyperactive-impulsive traits appear related to the restrictive-repetitive behavior domain in older children (Martin, Hamshere, O'Donovan, Rutter, & Thapar, 2014), and in adults the restrictive-repetitive behavior domain showed the strongest association with both dimensions of ADHD, on a phenotypic, genetic and environmental level (Polderman, Hoekstra, Posthuma, & Larsson, 2014). In the same line, aggregation of ADHD subdomains into one factor may have led to underestimation of genetic overlap in 2 year old twins. This possibility warrants consideration in light of the specific associations appearing between ADHD inattention and ASD, and the relative genetic specificity of the ASD domains (Happe & Ronald, 2008; Robinson et al., 2012) and to a lesser extent ADHD domains (Greven, Rijsdijk, et al., 2011; Nikolas & Burt, 2010).

The confounding effects of tests procedures may be stronger at young age. For example, the multifaceted composition and prolonged maturation of EF, make performance on EF tasks highly susceptible to the confounding effects of test procedures during early age, casting doubt on whether EF as measured with current neuropsychological tests across this age range has similar content validity. These

confounding factors have been relatively disregarded in many studies but are now increasingly subject to systematic investigation in eye tracking studies. In early childhood, eye tracking allows to study reflexive and conscious cognitive functions prior to the development of controlled behaviors. Eye tracking has amply been applied in infants at risk for ASD (see for reviews (Falck-Ytter et al., 2013; T. Gliga, E. J. H. Jones, R. Bedford, T. Charman, & M. H. Johnson, 2014b; Guillon et al., 2014; Sacrey, Armstrong, Bryson, & Zwaigenbaum, 2014). Using eye tracking, the experimental contexts can easily be manipulated. For example, by examining attention to a social scene versus to a screen in HR-infants with later ASD (Chawarska, Macari, & Shic, 2013); or attention during episodes involving dyadic cues that were directed or not directed at the child (Chawarska, Macari, & Shic, 2012). In the same line, the influence of task complexity on performance has been confirmed in many eye tracking studies in ASD where saccadic reaction time shortens with lower complexity (e.g., in gap- versus overlap tasks, with static- versus dynamic stimuli or with repeating versus varying stimuli) (see review by (Sacrey et al., 2014). Unfortunately, research with visual attention tasks in ADHD has mostly been performed from school age, and is based on different paradigms than in ASD (Rommelse, Van der Stigchel, & Sergeant, 2008). Interestingly, one study has found that attention (mean fixation duration) measured with eye tracking at about 7.6 months of age was positively related to temperament effortful control and negatively with hyperactivity-inattention behaviors at about 4.5 years of age (Papageorgiou et al., 2014), suggesting some continuity between infant and preschool attentional and behavioral control.

In summary, complex EF tasks in young children with ASD and ADHD measure many different components related to context and complexity and that may be a consequence of more basic regulatory and cognitive processes. To tease these components apart, the use of simple tasks and eye tracking is a promising line of research. In particular, eye tracking enables to characterize the core pathology “at a unique intermediate level”, in the sense that findings can be linked to everyday observable simple and complex behaviors, emotions and functions and to basic neuro-cognitive processes, autonomic responses; further, eye tracking can be used to investigate spontaneous behaviors and preferences in complex rather naturalistic situations (Falck-Ytter et al., 2013).

7.3. Interactions among systems

A challenge in the understanding of early development is to acknowledge that factors do not operate separately, and that it is crucial "to model complex interactions among systems and over time" (Johnson, 2011; cited by Elsabbagh et al. 2011). In the case of developmental disorders, it is assumed that the symptoms may be a result of early brain adaptations to genetic and environmental processes rather than a direct consequence of fixed neural pathology (Johnson, Jones, & Gliga, 2015). The reviewed literature supports the notion that symptoms, temperament and EF have to be interpreted in the context of the developmental systems they interact with, and that these interactions change and become increasingly compounded over time. For example, the moderating effect of a risk factor on symptom severity tends to become reciprocal in the course of preschool age, as well as the effect of symptom severity and IQ on rates of co-morbid problems. The temperament and cognitive data show that sensory/perceptual features, affective, effortful and cognitive control operate as precursors or risk factors for ASD and/or ADHD through interactions with each other and with genetic risk (Becker et al., 2010). These effects may confound primary with secondary causes and ultimately complicate the search for intervention targets. Treatment targets should therefore be sought in the multiple processes that mediate the disorders rather than in fixed core deficits and symptoms, which means a shift from developmental outcomes to causal processes (Sonuga-Barke & Halperin, 2010).

7.4. Areas for further research

The reviewed literature shows that the ASD and ADHD fields may greatly benefit from one another. In ASD, this includes the extension of early trajectories into preschool ages, and increase of research on executive functioning and on early environmental factors. In ADHD, this includes the downward extension of trajectories by studying infants at risk, and increased research on precursors or basic behavioral and cognitive components. In both conditions, there should be more attention for the role during early development of processes that fall outside the core deficits, like sensory and affective processes.

Neurobiological and environmental factors have been relatively disregarded in relation to early symptoms, temperament and cognition in ASD or ADHD. Although these areas fall outside the scope of this review, we briefly discuss them in light of the critical need for a multi-method approach in neurodevelopmental disorders.

Recent findings suggest that differences in brain function precede the overt behaviors symptoms in autism (Elsabbagh & Johnson, 2010). Mixed results were reported for deviances in early brain growth in relation to ASD and ADHD, with indication for brain volumes being increased in ASD and decreased in ADHD, but with still unknown early brain-growth trajectories and underlying processes (see reviews by Gliga et al., 2014a and M. H. Johnson et al., 2014). Recent reviews further support the assumption of brain wide atypicalities in ASD (Allely, Gillberg, & Wilson, 2014) and in ADHD (Castellanos & Proal, 2012; van Ewijk, Heslenfeld, Zwiers, Buitelaar, & Oosterlaan, 2012), and show that brain research in ASD covers an earlier age than in ADHD where most work has been performed from about school age. Research on early (brain) development calls for the use of non-invasive techniques that can more easily be applied in very young children like EEG and (functional) near infrared spectroscopy (Lloyd-Fox, Blasi, & Elwell, 2010), in addition to (functional) magnetic resonance imaging (MRI) (Wolff et al., 2015). Taking this into consideration, research on early brain development in ASD and ADHD might greatly benefit from the inclusion of behavioral, cognitive, physiological and also genetic measures that can be linked to brain function.

Although environmental factors are not considered as causative in ASD and/or ADHD by themselves, they may act as risk or protective factors during sensitive developmental periods beginning in prenatal life through interactions with child characteristics, particularly in (genetically) susceptible individuals (Gardener, Spiegelman, & Buka, 2009; Hartman & Belsky, 2015; Pluess & Belsky, 2011; Sonuga-Barke & Halperin, 2010). During the embryonic stage intrauterine environmental influences are likely to modulate risk for developmental disorders (Gardener, Spiegelman, & Buka, 2011; Hallmayer et al., 2011). One promising line of research is that of maternal early prenatal infections increasing the risk for ASD in the offspring (Atladottir et al., 2010) suggesting that a hypoactive immune cell activity is one

possible mechanism in children who later develop ASD (Abdallah et al., 2012). For the social environment, the caregiver is a known potential (dys)regulator and moderator of risk during early child development (Rothbart et al., 2011); Zeanah & Zeanah, 2009), whereby the child's difficulties or behavior problems can elicit compensating or negative parenting behaviors (Kiff, Lengua, & Zalewski, 2011). For example, behavior problems (Estes et al., 2013) and sensory problems (Ben-Sasson, Soto, Martinez-Pedraza, & Carter, 2013) in toddlers with ASD were associated with parental distress/family life impairment and stress. A recent study showed that infant interactive behaviors and dyadic parent-infant mutuality in interaction at 12 months were able to predict ASD outcome (Wan et al., 2013). For ADHD, findings suggest that low levels of parental sensitivity/ responsivity in preschoolers uniquely predicted later ADHD behaviors, an effect that may partly be due to parents' own ADHD (Keown, 2012). Early interventions studies focusing on parent-child interaction and parenting suggest that the effects primarily reside in improvement of parenting (and parent wellbeing) and decrease in co-occurring child problems rather than in decrease of core symptoms (Daley et al., 2014; Oono, Honey, & McConachie, 2013). This indicates that early transactional processes in ASD and ADHD are promising areas for further research, including intervention research. This research area calls for methods that are well suited to examine complex bidirectional effects longitudinally (Kiff et al., 2011), that control for psychopathology in all interaction partners and use genetically informed designs.

7.5. Genetic research

Quantitative genetic research on shared genetic influences on ASD and ADHD has mostly been conducted in older children and adolescents with ASD and ADHD, with few studies having performed cross disorder analyses (see for review Rommelse, Franke, Geurts, Hartman, & Buitelaar, 2010). Family and twin studies indicate substantial shared genetic factors of ASD and ADHD (e.g., Musser et al., 2014; Ronald at al., 2014; Taylor et al., 2015; Lichtenstein et al., 2010). In contrast, only modest phenotypic correlations between ADHD and ASD traits and also modest overlap of genetic factors were found in a population-based sample of 2 years old twins (Ronald, Edelson, Asherson, & Saudino, 2010). This smaller

genetic overlap may be due to measurement problems at very young age. Further, genetic loading for complex traits may be age-dependent and lower in the first years of life (Ronald, Edelson, Asherson, & Saudino, 2010).

Genome-wide association studies (GWAS) using common DNA variants (SNPs) allowing for the examination of share genetic etiology between disorders at the molecular level have found lower heritability estimates of ASD and ADHD problems in comparison to family or twin studies (Trzaskowski, Dale, & Plomin, 2013). Explanations for this heritability gap may be the lack of power to detect common associated variants of small effect due to relatively small sample size. Another explanation is that common DNA variants only capture additive genetic effects associated with complex behavioral traits, while not capturing gene-gene and gene-environment interactions, and rare alleles (Lee et al., 2013). This is relevant as molecular genetic studies have identified an increasing number of rare variants associated with developmental disorders as ASD, ADHD and/or intellectual disability that seem to converge in a limited number of neurobiological pathways (Vorstman & Ophoff, 2013). Genome-wide genotype data from the Psychiatric Genomics Consortium (PGC) for cases and controls in ASD and ADHD further allow for the examination of share genetic etiology of these two disorders at the molecular level (Lee et al., 2013). The non-significant genetic correlation that was found between ASD and ADHD (in contrast to genetic correlations between several other disorders) may be due to the samples sizes for ASD and ADHD being much smaller than for the other disorders in the PGC.

Genetic research on complex psychopathological phenotypes in the first years of life is sparse. However, quite some research has been done on basic psychological traits. This is highly relevant because finding genetic associations with basic traits, i.e., before they are confounded by interactions with other systems, might be easier (Papageorgiou & Ronald, 2013). Most studies have used a candidate gene approach with either dopamine, serotonin or cholinergic related genes and found differential but not fully consistent genetic associations with temperamental and attentional domains (for review, see Papageorgiou & Ronald, 2013). The most consistent finding has been a relation of a dopamine receptor D4 gene variant (L-DRD4) with several positive temperamental traits during infancy (e.g., better orientation, better response

to novel situations, higher activity, lower negative affect) but also with negative traits in this age range (e.g., shorter duration of looking/ latency of looking away, and also higher negative affect). One longitudinal study has found that the L-DRD4 genotype in combination with regulatory problems in infancy was predictive of middle childhood ADHD (Becker et al., 2010).

Several explanations are presented for the inconsistent genetic findings across these studies that are related to age, measurements and possible interactions with the environments (see also review by Papageorgiou & Ronald, 2013). Inconsistencies between studies that differ in age range may reflect changes in the genetic underpinnings of a domain. In addition, different underlying mechanisms may be involved in a trait at different ages. For example, cholinergic systems involved in attentional orienting may only foster regulation during early infancy, whereas later on regulation may pass to the executive control network (Posner, Rothbart, Sheese, & Voelker, 2012) cited in (Papageorgiou & Ronald, 2013). Further, different methods of measurement, e.g., questionnaire, test or observation, may tap different underlying constructs. For example, genetic correlations in 2 years old twins suggested that activity level (AL) at home at this age shows more overlap with ADHD behavior than AL in the lab, supporting the separation of the three measures for molecular analyses (Ilott, Saudino, Wood, & Asherson, 2010). Further, children may differ in their susceptibility for the quality of their environments based on their genotype (Belsky & Pluess, 2009).

In line with the aforementioned challenges and recommendations, future genetic research on unique and shared etiology between ASD and ADHD should take account of the effects of age/development stage on measurements and acknowledge eventual changes in underlying constructs. In this regard, basic phenotypes and functions might more easily be linked to genetic factors than composite phenotypes and functions. Further, examining contextual influences within (i.e., genetic effects that are situation-specific such as activity level in a familiar vs unfamiliar environment), and across individuals (due to gene-environment interactions/differential susceptibility) is essential to unravel genetic and environmental components (Saudino & Micalizzi, 2015). This requires a multi-method approach to measurement. Finally, the combined study of multiple phenotypes and multiple genes is warranted to elucidate the associations and interactions between them. In this way, polygenic risk scores for ASD and ADHD might be mapped

onto early measures of ASD and ADHD. This might be helpful to further clarify the role of unique and common genetic etiology on the phenotypic overlap between ASD and ADHD early in life.

8. Clinical implications

This review provides a basis for several clinical implications regarding assessment, early recognition and treatment recommendations for co-occurring ASD and ADHD. In view of the strong clinical overlap, children referred for ASD should also be assessed for ADHD (traits) and vice versa, which also implies that clinicians should look for ASD problems in the context of ADHD and for ADHD- and emotion regulation problems in ASD.

Given the complex and prolonged developmental trajectories in many function domains and increasing co-occurrence of ASD and ADHD between infancy and preschool age, clinical diagnostic assessments should be repeated over time. From early age, assessments should in any case cover attentional functions in different contexts as dysfunctions in these domains appear a risk marker for -and linking pin between- ASD as well as ADHD.

Temperament and EF are very useful trans-diagnostic specifiers that are likely to moderate clinical outcome (Johnson, 2012; Karalunas et al., 2014). In this regard, temperament measures related to neurobiological systems (Rothbart's scales) are preferable in order to capture (1) rather stable basic response traits of approach and withdrawal and their underlying motivation (manifested through sensory, affective and behavioral features) and (2) regulatory or effortful control traits (including duration of orienting/attentional focus, inhibitory control and shifting), which traits are differentially associated with the heterogeneous phenotypes of ASD and ADHD. As EF in young children largely depends on age at assessment and type of EF measures, the challenge is to use methods that allow for a distinction between deficits and normative variations in maturation. In infancy (about the first 1.5 year) and toddlerhood (between about 1.5-3 years), EF-related temperamental regulation behaviors may most easily be assessed

by the Revised Infant Behavior Questionnaire (IBQ-R; Gartstein and Rothbart, 2003) and Early Childhood Behavior Questionnaire (ECBQ; Putnam et al. 2006), respectively. Although basic reflexive and non-controlled cognitive functions in very young children can most reliably be measured with eye tracking, the method is not readily available for clinical assessment purposes because normative data are lacking and the predictive validity regarding clinical diagnosis is not established enough. In infants and toddlers, clinicians should also consider the use of simple tasks for basic EF components in the domains of attention (e.g., look duration and shift rate), processing speed (e.g., psychomotor- and encoding speed), and memory (e.g., immediate- and delayed recognition) that are associated with later EF (Rose et al., 2012). Further, varying the test conditions by using different types of targets, distractors and instructions, may help isolate EF impairments from confounding factors such as sensory- and social information processing difficulties, affective control and motivational processes.

In order to rightly interpret individual characteristics and decide to which extent these may be attributed to ASD, ADHD or an overlapping spectrum, it is critical to (1) search for early signals specific to ASD or ADHD in the developmental history, (2) examine whether the motivational and contextual correlates of sensory- cognitive and behavioral symptoms are differentially pointing to ASD or ADHD, and (3) examine the effect of developmental course and effect of interventions as these may uncover the most salient pathology.

Given the pivotal role of early attentional functioning in ASD and ADHD, the further development of (preventative) interventions beginning in infancy and focusing on training of attentional functions has a high priority (Wass, Porayska-Pomsta, & Johnson, 2011). In the same line, training of executive functioning using activities, exercises and games and improvement of emotional regulation (e.g., identifying and articulating feelings, anger management) beginning at early preschool age are promising interventions with potential preventative effects (Halperin et al., 2013; Rabinovitz et al., 2016; Wass, 2015; Webster-Stratton, Reid, & Beauchaine, 2011).

While outside the scope of this review, we finally want to stress the importance of involving caregivers in early interventions for more effective generalisation of developmental gains in multiple

settings (Wallace & Rogers, 2010). Moreover, the difficulties of the child in the core- and related domains place a burden on caregivers and may also undermine their competence and sensitivity (Davis & Carter, 2008). Therefore, early interventions should include psychoeducation and concentrate on optimising interactions between child and caregivers, preferably before interactions become embedded in emerging social atypicality (Wan et al., 2013), disregulated behaviors and coercive patterns.

Conclusions:

Several preliminary conclusions can be drawn from this review on the shared or unique early behavioral and cognitive characteristics of ASD and ADHD: 1) core symptoms or traits of ASD and ADHD frequently co-occur, and this co-occurrence increases with age, severity of symptoms and lower IQ; 2) attentional problems form a linking pin between ASD and ADHD but the behavioral, cognitive and sensory correlates partly diverge between the two conditions; 3) ASD and ADHD share high levels of negative affect as a temperament trait, although the motivational mechanisms diverge (i.e. withdrawal versus approach in ASD vs ADHD, respectively); and 4) ASD and ADHD share difficulties with control and shifting, but partly opposite behavioral tendencies seem to be involved. These conclusions are inferred from a disparate literature and sometimes limited data wherein age effects are often not clearly understood, therefore requiring more research.

To understand the causative mechanisms of the early ASD and ADHD pathways and of the links between ASD and ADHD, methods have to be used that allow to bridge the gaps between the divergent ASD and ADHD research fields, between basic and compounded functions across developmental periods beginning in prenatal life, and between these functions and their neurobiological foundation. Further, a large variety of interacting processes are implicated in the pathways of neuro-developmental disorders. This calls for a multi-method approach wherein a large range of behavioral, cognitive and gaze/sensory processing measures are combined with neurobiological measures including the use of state-of-the-art non-invasive methods to assess brain structure and function, and including early social and biological environmental factors.

Ultimately, these insights will inform intervention research and lead to a re-shift in focus away from rather fixed developmental/diagnostic outcomes to more causal processes (Gliga et al., 2014a; Sonuga-Barke & Halperin, 2010).

Conflict of interests.
Dr. Buitelaar has been a consultant to / member of advisory board of / and/or speaker for Janssen Cilag BV, Eli Lilly, Shire, Medice, and Servier. He is not an employee of any of these companies, and not a stock shareholder of any of these companies. He has no other financial or material support, including expert testimony, patents, royalties.

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Fig. 1. Temperament traits in ASD and ADHD: ASD and ADHD share high levels of negative affect, but the underlying motivational and behavioral tendencies seem to differ, i.e. withdrawal versus approach in ASD vs. ADHD, respectively. ASD and ADHD also share difficulties with control and shifting, but partly opposite behaviors seem to be involved, i.e. high persistence and low distractibility in ASD and poor sustained attention and high distractibility in ADHD.

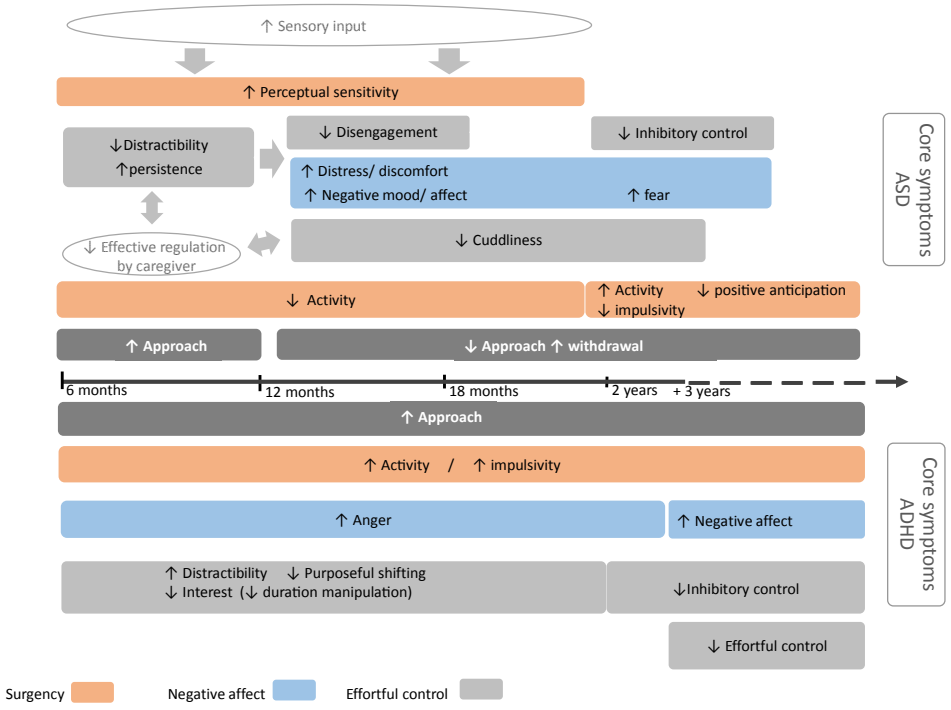

Table 2

Summary of findings on temperament in children with (traits of) ASD or ADHD.

	6-11 months		1-2 years		2-3 years		3- 4 years		4-5 years	
Temperament dimension	**ASD**	**ADHD**	**ASD**	**ADHD**	**ASD**	**ADHD**	**ASD**	**ADHD**	**ASD**	**ADHD**
APPROACH/SURGENCY										
Composite score	↑[2,3*b]		↓[2]		↓[2,3*] ns[12]		↓[3*]	↑[9]		↑[9]
Activity	↓[1,3*,5]	↑[7,8]	↓[3*]	↑[8]	↑[1,4]	↑[8]	↑[6] ↓[12 e]		↑[6] ↓[12 e]	
Perceptual sensitivity	↑[2]	ns[7]	↑[2]	ns[7]		ns[7]				
High intensity pleasure	↓[2]							↑[10]		↑[10]
Positive affect			↓[2]		↓[4]					
Positive anticipation/ non-shyness [a]					↓[4 c]		↓[6]		↓[6]	
Impulsivity							↓[12 e]	↑[10]	↓[12 e]	↑[10]
NEGATIVE AFFECT										
Composite score	ns[3*]		ns[3*]		ns[3*] ↑[12]		ns[3*]	↑[9,11]		↑[9]
Sadness/shyness [a]	↑[1]				↑[1,2,4]	↑[8]			↑[12]	
fear		ns[7]		ns[7]	ns[12]	ns[7]	↑[12]		↑[12]	
Anger		↑[7]		↑[8]	↑[4]	↑[8]				
Distress/ discomfort reactions		↑[13]	↑[5]		↑[12]					
EFFORTFUL CONTROL										
Composite score			↓[2]		↓[2] ns[12]		ns[12]	↓[9,10]		↓[9,10]
Persistence/ non-distractibility	↑[1] ns[3*]		ns[3*]		↑[1] ns[3*]					
Vigilance/ interest (ADHD)		↓[7d, 8]		↓[8]		↓[8]				
Cuddliness			↓[2]		↓[2]					
Low intensity pleasure					↓[2]					
Attention shifting		↓[8]	↓[5]	↓[8]	↓[4,5]		↓[12]		↓[12]	
Control of attention					↓[4]	↓[8]				
Inhibitory control					↓[5]	↓[8,14]	↓[12 e]	↓[13]	↓[12 e]	

Note: ASD = high scores on questionnaires or ASD diagnosis (at 3 years or older) or, high risk children (HR) who later received a diagnosis ASD (HR-ASD); ADHD = high scores of ADHD symptoms on questionnaires or in a few studies clinical diagnoses; 3*: in study 3 (Del Rosario et al., 2013) HR-ASD were only compared to HR non-ASD without low risk group; [a] : shyness: is component of negative affect in infants and toddlers, and component of approach/surgency in preschoolers and older; [b] : High approach in infancy in study 3 referred to social and non-social stimuli (=low inhibition); [c] : in study 4 high positive anticipation was found in HR non-ASD; [d] : ↓interest = duration orienting and manipulation of objects; [e] : Lower activity and -impulsivity (=lower approach and lower response speed) associated with more social impairments. Empty cells: not tested.

[1] Bolton et al., 2012; [2] Clifford et al., 2013; [3] Del Rosario et al., 2013; [4] Garon et al., 2009; [5] Zwaigenbaum et al., 2005; [6] Brock et al., 2012; [7] Auerbach et al., 2004; [8] Auerbach et al., 2008; [9] Martel et al., 2012; [10] Miller et al., 2013; [11] Healey et al., 2011; [12] Salley et al., 2013; [13] Dougherty et al., 2011; [14] Gagne et al., 2011.

Appendix. Table 1. Co-occurrence of core ADHD and ASD symptoms/traits in studies with young children with ASD or ADHD (traits).

Reference	Design/ Sample N, Group/ Sample	Age years (y) or months (m) Mean (range*) / Percentage boys	Domain(s) investigated/ Remarks	Assessment and diagnostic	Main findings
Carlsson et al., 2013	CS; Clinical (early ASD intervention sample); N=198 (AD, n=106; ASD-like, n=58, Asperger, n=13; ASD traits, n=21) Examined co-occurring disorders.	4.5y–6.5 y 85% boys	Co-occurring disorders in ASD (ADHD diagnosis/ or severe -problems). No formal testing for ADHD	ASD diagnosis: DSM-IV criteria; DISCO Tests: cognitive; language Co-occurring problems (Activity Regulation and Behavioral Problems) by parent interview, and including severe hyperactivity/diagnosis ADHD	Severe hyperactivity or diagnosed ADHD (parental interview) reported in 63/198 children (32%).
DuPaul et al., 2001	CS; Clinical; N= 94 (ADHD, n=58, typical controls, n=36) Examined difference in functioning between preschool-age children with ADHD) and control children.	4y (3-5) ADHD: 86 % boys Control: 55% boys	Social competence Items of PKBS are not specific for ASD	ADHD: CPRS-R; SIDAC; DSM-IV. Social Skills: PKBS (Social Skills subscales: cooperation, interaction, independence and Problem Behavior subscales)	Children with ADHD exhibited more problem behavior, were less socially skilled and exhibited more negative social behavior in preschool settings than controls.
Fodstad et al., 2010 .	CS; Clinical (N=269): atypically developing toddlers: ASD (n=109), non-ASD (n=160) Investigated comorbidity in children with ASD.	4 age groups for ASD and atypical control groups: 1.5y (1-1.6), 1.8y (1.7-2), 2.3y (2.1-2.6), and 2.8y (2.7-3.2).	ADHD symptoms	ASD: CBE; DSM-IV; M-CHAT, BISCUIT-Part 1 ADHD symptoms: BISCUIT-part 2 Developmental test: BDI-2	Toddlers with ASD had more severe symptoms than atypically developing non-ASD toddlers. Comorbid problems can emerge at 1y of age, increase to problematic levels from 2.1y–3.3y of age; increasing trend of comorbid behaviors as age increased.
Gadow et al., 2004	CS; Clinical: PDD (n=172/160 [*]), non-PDD referrals (n=135/101 [*]), typical (n=507/407[I]), and early childhood programs sample (n=64/140 [*]) Investigated comorbidity in children with ASD. [*] parent/teacher ratings	4.6y (3-5)	ADHD diagnosis	ASD: CBE based on comprehensive assessment and ECI-4 ADHD: ECI-4	± 40% of the children in the ASD sample met DSM-IV criteria for ADHD. ASD sample was as inattentive as the non-ASD clinic group, and both clinic samples were more inattentive than the regular and special education samples. Differences were largely accounted for by differentially higher rates of ADHD-inattentive than ADHD-hyperactive/impulsive subtype symptoms.
Gadow et al., 2006	CS; Clinical ASD (n=182); Control non ASD (n=135) Compared DSM-IV ADHD subtypes in children with ASD	ASD: 4.2y (3-5) Non ASD: 4.6y (3-5)	ADHD diagnosis	ADHD: ECI-4; CBCL; TRF	The Inattentive group was more socially and language impaired than the Hyperactive-Impulsive group. Differences between subtypes are complex, even within domains of functioning (e.g. impairment in social

	versus non-ASD clinic referrals.				performance varied by measure (Peer Conflict Scale, Conduct Disorder, and Social Deficits symptom).
Georgiades et al., 2011	CS; Clinical (N=335) newly-diagnosed with ASD. Examined phenotypic overlap between core diagnostic features and emotional/ behavioral problems in children with ASD.	3.3y (2–4) 85% boys	Emotional/ behavioral problems including attention problems	ASD: DSM-IV criteria and ADOS and ADI-R Behavioral problems: CBCL Repetitive Behavior Scale-Revised (RBS-R). Developmental test/adaptation: M-P-R; PLS-4; VABS	Children with ASD had high scores on the Withdrawn, Attention Problems, and Emotionally Reactive domains compared to the norms. Structure of this expanded ASD clinical phenotype had two independent components: Emotional-Behavioral-Repetitive and Social Communication Deficits. CBCL Withdrawn and Attention subscales loaded relatively high on both components.
Hartley et al., 2008	CS; Clinical (N=169) children with AD. Examined prevalence of clinically significant maladaptive behaviors and risk factors in the child for maladaptive behaviors.	3.5y (1.5–5.8) 78% boys	Emotional/ behavioral problems including attention problems	Diagnosis AD: comprehensive assessment and ADOS-G; Developmental test/adaptation: MSEL; VABS Co-morbidity: CBCL	1/3 of children with AD had CBCL-Total Problems score in clinical range. Highest percentage of clinically significant scores were in Withdrawal, Attention, and Aggression CBCL scales. Clinically significant attention problems were reported for 38.5% of children with AD. Strongest predictor of externalizing behavior was non-verbal cognitive ability.
Horovitz & Matson, 2013	CS; Clinical: early intervention sample (N=2867) for developmental delays including medical conditions and ASD. Developed age-based cutoff scores for comorbidity questionnaire and compared them to full-sample cutoff scores.	2.2y (1.5–3.1) Separation in 3 age cohorts: 1.5-1.11 y, 2y-2.5y and 2.6y-3.1y	ADHD/disruptive symptoms	ASD diagnosis: CBE using DSM-IV criteria, M-CHAT, BDI-2 ADHD/disruptive symptoms: BISCUIT-Part 2 Developmental test: BDI-2	Symptoms of co-morbidity became more pronounced and easier to detect with age in toddlers with ASD but not in children with non-ASD related atypical development. Highest co-morbidity domains: tantrum/ conduct behavior and inattention/ impulsivity. Mean BISCUIT Inattention/impulsivity score (ASD versus non-ASD atypical): 1.5-1.11yr = 7.71 versus 1.89 2-2.5yr = 8.59 versus 2.21 2.6-3.1yr = 10.19 versus 1.92
Lecavalier et al., 2011	CS; Clinical ASD (N=229) Determined if the symptoms of ADHD, ODD, and Mood aggregated in a manner consistent with DSM-IV nosology, using CFA.	4y (3–5) 78% boys	Comorbidity, including ADHD symptoms	ASD: CBE using developmental history, observations, previous evaluations, ECI-4; 37% ADOS Co-morbidity: ECI-4.	Correlation between ASD severity and ECI-4 factors were in the low to moderate range, with the strongest associations with ADHD-Inattention. Most symptoms loaded on their respective syndromes with the exception of ADHD Hyperactive-Impulsive factor (possibly due to underreport of verbal HA-Impulsivity items).

Matson et al., 2009	CS; Clinical either autism or PDD-NOS (N=309) and atypical developing children without ASD (N=461). Examined comorbid psychopathology.	ASD group: 2.3y (1.5–3.1) 73% boys Atypical control group: 2.2y (1.4-3.1) 68.4% boys	Externalizing (incl. ADHD) and internalizing problems	ASD diagnosis: CBE using DSM-IV criteria, M-CHAT, BDI-2. ADHD symptoms: BISCUIT-Part 2; Developmental test: BDI-2	All five disorders (tantrum, conduct behavior, inattentive/impulsive, avoidant behavior, anxiety/repetitive and eating problems/sleep) were more common in the autism group. Items rated as moderate to severe problem or impairment for ≥50% of the total ASD population fell under the Tantrum/Conduct behavior and Inattention/Impulsivity subdomains.
Matson et al., 2010	CS; N=342 (AD=119; PDD-NOS=116; DD control=107); Examined comorbid psychopathology in infants and toddlers with autism and PDD-NOS.		Externalizing (incl. ADHD) and internalizing problems	ASD diagnosis: CBE using DSM-IV criteria, M-CHAT, BDI-2. Comorbidity: BISCUIT-Part 2; Developmental test: BDI-2	Differences between all groups on all factors of comorbidity were significant aside from factors avoidance behavior and anxiety/repetitive behavior between the PDD-NOS and control groups. The AD group exhibited the highest scores on each of the subscales, followed by the PDD-NOS group, and the control group scoring the lowest on all subscales.
Matson et al., 2010	CS; clinical ASD (N=198) Two levels of developmental quotient: (1) low (less than or equal to 70; n = 80), and (2) typical (greater than 70; n = 118). Examined the effect of developmental quotient on symptoms of inattention and impulsivity.		ADHD symptoms	ASD diagnosis: CBE using DSM-IV criteria, M-CHAT, BDI-2. ADHD symptoms: BISCUIT-Part 2; Developmental test: BDI-2 Symptoms of inattention and impulsivity: BISCIUT-Part 2 inattention/impulsivity subscale.	No significant effect of developmental quotient on inattention/impulsivity items when severity of ASD was controlled for. Severity of ASD symptoms, was significantly related to 12 of the 14 inattention/impulsivity items.
Ronald et al., 2010	CS; Population, twin design (N=312 pairs of twins). Examined co-variation of ASD and ADHD traits and extent to which co-variation is explained by genetic and environmental influences.	2.1y (SD=0.05)	Co-variation ASD and ADHD traits	Autistic like traits: CBCL PDP scale (Social Communicative and Non-Social subscales); ADHD traits: CBCL ADHP subscales; Developmental test: BSID-II.	Autistic-like traits (social and nonsocial subscales) correlated with ADHD behaviors (r=0.23–0.26). Co-variation was caused by a modest proportion of common genetic influences (r=.27) across autistic traits and ADHD behaviors as well as by common shared environmental influences. For autistic traits, social and nonsocial traits are equally associated with ADHD behaviors and both contribute to the modest genetic overlap between these two categories of behavior.
Sikora et al., 2012	CS; Clinical multisite ASD sample (N=3066); 2-5yr ASD subsample (N=1737) Evaluated frequency of co-occurring ADHD	Age range whole sample=2y–17.9y (data reported for subsample of 2-5y olds). 84% boys in whole sample	ADHD symptoms	ASD diagnosis: ADOS and/or DSM-IV symptom checklist; ADHD symptoms: CBCL (AP and ADH problems scales as categorical variables (score <70 versus ≥ 70); Adaptive Behavior: VABS-II	39.3% of children received T scores >70 on only 1 subscale (either the AP scale or ADHP DSM-oriented scale). Over 18.8% had elevated T scores on both subscales. The ASD + ADHD group had lower scores on the VABS-II in comparison with the ASD alone group.

	symptoms in school- versus pre-school children with ASD.			Cognitive: MSELor Stanford-Binet	*Parents of preschoolers reported significantly less ADHD symptoms than parents of school-aged children.*
St.Pourcain et al., 2011	LG; Population (N=5383). Examined the interrelations between trajectories of autistic and ADHD traits.	Hyperactive-inattention traits: at 4y-7y-8y-10y-12y-13y-17y Autistic traits : **8**-11-14-17y 49% boys	Autistic and ADHD traits	Hyperactive-inattention traits: SDQ Autistic traits: SCDC	LCG analysis revealed 2 distinct social communication trajectories (persistently impaired versus low-risk) and 4 hyperactive-inattentive trait trajectories (persistently impaired, intermediate, childhood-limited and low risk). Trajectories for both traits were strongly but not reciprocally interlinked: majority of children with a persistent hyperactive-inattentive symptoms also showed persistent social-communication deficits but not reverse.
Thorell et al.,2008	CS; Population: pre-school (*n*=29) and school-aged children (*n*=31) high in ADHD symptoms (total *N*= 60) and control group of preschool (*n*= 238) and school-aged (*n*=261) children (total *N*= 499). Examined effects of age and gender on behavior problems and social competence in preschool and school-aged children high in ADHD.	4y–4.11y versus 9y-9.11y 62% boys in high ADHD group 50% boys in control group	ADHD symptoms Social competence Externalizing and internalizing problems	ADHD symptoms: ADHD Rating Scale IV (cut-off=4 symptoms of hyperactivity/impulsivity or inattention) ODD symptoms: DSM-IV Externalizing and internalizing problems: CBQ; Social competence: SCI	Children high on ADHD symptoms differed control group with regard to most measures: -Lower levels of *prosocial orientation* -Higher number of ODD symptoms -No difference in *social Initiative.* No significant main effects of age or interactions of ADHD symptoms and age suggest that preschool and school-aged children high on ADHD symptoms have similar behavior profile.
Tureck et al., 2015	CS; Clinical: early intervention sample for developmental delays or a medical condition (N=2300). Examined how severity of ASD symptoms predicts ADHD symptoms in atypically developing toddlers.	1.5y-3.1y (mean and SD not reported) 70% boys	Severity autistic and ADHD symptoms	ASD symptoms: BISCUIT-Part 1 ADHD symptoms: BISCUIT-Part 2; Developmental test: BDI-2	Severity of ASD symptoms was significantly and positively related to all 16 items of the Inattention/ Impulsivity subscale. The largest effect was for *Concentration problems*.
Turygin et al., 2013	CS; Clinical: early intervention sample for developmental delays or a medical condition (N=2956); ASD (n=656). Examined prevalence and characteristics related to ADHD diagnosis in toddlers with ASD versus at risk of developmental delay.	Age at assessment not reported; Whole sample: 71% boys ASD: 74% boys	ADHD symptoms	ASD diagnosis: CBE using DSM-IV criteria, M-CHAT, ADHD symptoms: BISCUIT-Part 2 Developmental test: BDI-2	Prevalence rates for ADHD in the overall sample was 4.50%, and prevalence rates by gender, race, and presence of ASD were comparable. The prevalence was not significantly different in children with an ASD diagnosis.

Table 2

Executive function in studies with young children with ASD or ADHD (traits).

References	Sample	Age range (Mean) in years	Domain(s) investigated	Assessment and diagnostic	Main findings
Berwid et al., 2013	CS; Population: over recruited high in ADHD symptoms: Hyperactive/ inattentive (HI) (*n*= 148) or control (*n*= 120). Examine whether ADHD symptoms are associated with an early-emerging deficit in post error slowing.	4.4y (3.0 -5.4) HI 76.4% boys Control 60 % boys	Response monitoring (post error slowing)	ADHD: DSM-IV TR; BRIC (including items relevant to five behavioral domains: Attention, Activity Level, Impulsivity, Affect, and Sociability). Computerized Perceptual and Motor Conflict Test, modified for use with young children; IQ: Information subtest of WPPSI-R; or WPPSI-III.	HI children exhibited reduced post error slowing relative to controls on the trials selected for analysis. Supplementary analyses revealed that this might have been due to reduced proportion of trials following errors on which HI children slowed rather than due to a reduction in the absolute magnitude of slowing on all trials following errors. The results thus suggest that this deficit is perhaps more a result of failures to perceive errors than of difficulties with executive control.
Dawson et al., 2002	CS; Clinical; ASD (n=72); children with DD (n=34); typically developing children matched on mental age (n=39). Examined EF in children with ASD, and whether EF performance is correlated with ASD symptoms, and joint attention ability.	Clinical: 3-4y Control: 1- 3.8y	Executive functions (EF)	ASD: ADI-R; ADOS-G; clinical judgment of diagnosis based on DSM-IV. EF: Ventromedial Prefrontal (VMPC) tasks: Delayed nonmatching to sample and Object discrimination reversal. Dorsolateral Prefrontal (DLPC) tasks: A not B task; A not B with invisible displacement; Spatial reversal. Joint Attention: Butterworth	Children with ASD performed similarly to comparison groups on all EF tasks. Children with ASD performed worse on the joint attention tasks than did children with DD and typical development. VMPC task performance was related to joint attention ability, even after controlling for effects of mental age and level on joint attention ability. DLPC task performance was not related to joint attention Ventromedial, but not dorsolateral, prefrontal task performance was strongly correlated with joint attention ability.
Healey et al., 2011	CS; Population over recruited for ADHD: (n= 140) hyperactive/ inattentive; typically developing (n= 76). Investigated the moderating effects of cognitive functioning on relationship between negative emotionality and ADHD severity.	4.3y (3–4)	Neurocognitive functioning (Attention/Executive, Language, Memory, Sensorimotor, and Visuospatial). Temperament (negative emotionality)	Neuropsychological test: NEPSY; Negative emotionality: TABC-R; ADHD: ADHD-RS-IV	High levels of negative emotionality were associated with higher ADHD severity and lower Verbal & Executive Functions and Perceptual-Motor & Executive Functions. Both negative emotionality and Perceptual-Motor & Executive Functions accounted for significant unique variance in ADHD symptom severity. In the context of severe temperamental negative emotionality strong neurocognitive abilities do not seem as protective with regard to ADHD symptoms. With less severe negative emotionality, strong neurocognitive abilities place children at a clear advantage in relation to ADHD severity.

Kimhi et al., 2014	CS; clinical; ASD (n=29); TD (n=30). 1) Compared children with ASD and with TD on two EF abilities and on two ToM tasks; 2) test links EF with ToM.	ASD: 4.9y (SD=11) TD: 4.6 (SD=11) 86% boys	Executive functions: shifting and planning	ASD: DSM-IV criteria and ADI-R Developmental test: MSEL; EF: shifting (FIST); planning (TOL); ToM: unexpected location and false belief task.	Intellectually able children with ASD demonstrated difficulties on EF (cognitive shifting and planning) abilities and on most ToM prediction and explanation abilities, relative to matched typically developing preschool age children. In both groups, EF planning and cognitive shifting as well as VIQ contributed to better ToM explanation and prediction abilities.
Martel et al., 2013	CS, population over recruited, N=98 divided in 2 groups via multistage screening: DBD (*n* = 74), including ADHD-only (*n* = 17), ODD-only (*n* = 18), and ADHD+ODD (*n* = 39); and children without DBD (*n* =24). Evaluated association between control processes and ADHD and Oppositional Defiant Disorder.	4.3y (3-6) 57% boys	Cognitive control (EF) Temperament (Affective control and effortful control)	Cognitive control: Response inhibition (Shape School); simple and complex working memory (backward digit span); set-shifting (adaptation of TRAILS-P); Temperament: Affective control: CCQ; LABTAB (gift delay); Effortful control: composite scale score on CBQ	Affective control, but not effortful control, was associated with cognitive control. Decreased affective control (gift delay task) was associated with increased parent- and teacher-rated ADHD symptoms, specifically inattention (parents) and hyperactivity-impulsivity (parents and teachers). Worse response inhibition and working memory was associated with increased (teacher-rated inattentive ADHD symptoms, not parent rated symptoms. Worse set-shifting was associated with increased ADHD symptoms and inattention (parents and teachers).
Miller et al., 2013	LG; Population over recruited for ADHD (N=214): high in ADHD (n=138); low in ADHD (n=76). Examined relationship between temperament, neurocognitive testing and ADHD (via parents and teachers), both at baseline and 1 year later.	Time 1= 4.3y (3.0-5.0) Time 2= 5.4y 73% boys	Temperament	ADHD: (ADHD-RS IV) ; Temperament: CBQ. Neuropsychological test: NEPSY Latent factor of *cognitive control:* Attention-Executive domain (NEPSY), and Effortful Control index (CBQ). Latent factor *stimulus-driven processing:* Impulsivity and High Intensity Pleasure (CBQ)	Cognitive control processes, but not stimulus-driven processes, were related to inattention and hyperactivity at baseline and at follow up. In contrast, stimulus-driven processes, were related only to hyperactivity symptoms longitudinally. Overall, the results suggest that ADHD and its course over development may be highly influenced by distinct neural mechanisms associated with cognitive control and stimulus-driven processing.

Noland et al., 2010	LG; ASD-sibs (n=25); TD-sibs (n=30). Compared working memory (WM) for location of social vs. non-social targets in infant sibs-ASD (n=25) and typically developing children (sibs-TD, n=30) at 6.5 and 9 months of age.	6.6m visit: Age ± 6,6m (SD ± 7days) ASD-sibs n=19 73% boys TD-sibs n=22 74% boys 9m visit: 9.2m (SD ± 11days) ASD-sibs n=23 52% boys TD-sibs n=29 52% boys	Working memory Later ASD diagnosis of sibs-ASD not tested.	ASD-sibs: siblings of children with ASD (later ASD diagnosis was not tested); WM: task that challenged infants to remember location of social and non-social targets, and to update their WM across sequence of trials involving three different locations sampled with replacement-delayed-response task (a modification of the peek-a-boo game).	There was a significant interaction of risk group and target-type on WM: the sibs-ASD had better WM for non-social targets as compared to controls. There was no group by stimulus interaction on two non-memory measures. The results suggest that the increased competency of sibs-ASD in WM (creating, updating, and using transient representations) for non-social stimuli distinguishes them from sibs-TD by 9 months of age.
Pauli-Pott et al., 2013	CS; population: N=130 HR ADHD 20% (n = 26). Investigated to what extent executive Inhibitory Control (IC) and delay aversion (DA) mediate associations of familial, prenatal, and psychosocial risks with ADHD.	3-6y 50% boys	Executive IC and delay Aversion Familial, prenatal, and psychosocial risks	ADHD: structured interviews and questionnaires completed by parents and teachers. Prenatal risks: medical records. Psychosocial risks: structured interview. Neuropsychological tasks on IC (inhibitory control) and DA (delay aversion)	Familial, prenatal, and psychosocial risks were significantly associated with ADHD symptoms. IC and DA also correlated significantly with ADHD symptoms. While familial risk significantly correlated with IC and DA, psychosocial and prenatal risks were only weakly associated with these measures. The link between the familial risk and ADHD symptoms was partially mediated by IC and DA. In contrast, prenatal and psychosocial risks were largely independent of IC and DA.
Pellicano, 2010	LG; clinical: N=45: AD (n=31);PDD-NOS (n=12); Asperger (n=2). Examined relationships among theory of mind (ToM) and executive function (EF) in ASD.	T1: 5.6y (4.1-7.3) T2: 3 years later	Executive functions:	Executive functions: T1: planning ability (TOL, Mazes tasks), cognitive flexibility (set-shifting task), and inhibitory control (Luria's hand game). T2: cognitive flexibility (set-shifting task 2), and Tower of London task.	Individual differences in early EF predicted change in ToM skills over and above the variance that was accounted for by age, verbal ability, nonverbal ability, and initial ToM performance. In contrast, there was no independent relationship between early ToM skills and later executive control.

Rajendran, Rindskopf et al., 2013	LG; Over recruited H/I; (*n*=140) and typically developing children TD (n=76). Examined longitudinal associations (4 waves) between ADHD severity and neuropsychological functioning among children at high and low risk of ADHD.	T1: 4.3y (3-4) T2: 5.4y (4-5) T3: 6.3y (5-6) T4: 7.3y (6-7) Mean interval between assessments: 11.99, 11.65 and 11.80 months, respectively	Neuropsychological functioning: -Attention/Executive, -Language, -Visuospatial, -sensorimotor, -Memory	ADHD: ADHD-RS-IV (if (very) often score ≥6 =H/I; score<3 =TD); Neuropsychological functioning was measured annually using the NEPSY at four time points (mean ages, 4.2, 5.4, 6.3, and 7.35 y).	In the H/I group (and not in TD), improved neuropsychological functioning was associated with subsequent diminution of ADHD severity. In H/I and TD groups, there was inverse, reciprocal, longitudinal association between ADHD severity and neuropsychological functioning after the age of 4–5 years. Of lesser magnitude, greater ADHD severity at 5–6 years was associated with poorer neuropsychological functioning at 6–7 years.
Rajendran, Trampush et al., 2013	LG, Over recruited HR ADHD (N=138) (same as in previous ref). Investigated if changes in neuropsychological functioning were associated with the trajectory of ADHD symptoms/impairment.	4.2y, 5.4y, 6.3y, 7.3y, and 8.8y 75.5% boys at study entry	Changes in neuropsychological functioning Trajectory of ADHD symptoms	ADHD ADHD-RS-IV and CPC at 10 time points; Neuropsychological functioning: NEPSY (annually at four time points (mean ages, 4.2, 5.4, 6.3, and 7.35 y).	Baseline neuropsychological functioning was not significantly associated with the slope of change in ADHD severity. However, magnitude of change in neuropsychological functioning was linearly associated with the trajectory of ADHD symptom severity and impairment, such that individuals with greater neuropsychological growth over time had a greater diminution of ADHD severity and impairment. *Family socioeconomic status at baseline was significantly associated with initial ADHD severity and impairment, but not with change over time.*
Rohrer-Baumgartner et al., 2014	CS; Population N=1181. Tested if IQ-score influences associations between ADHD symptoms and verbal and nonverbal WM, inhibition, and expressive language.	3.5y (3.1-3.9) 52% boys	Nonverbal working memory, inhibition, and expressive language	ADHD: PAPA IQ and WM: subtasks from the Stanford Binet; Expressive language: CDI; Response inhibition : NEPSY;	There was interaction between ADHD symptoms and IQ on teacher-reported expressive language. In children with below median IQ-score, more ADHD symptoms were more likely to be associated with lower expressive language, while ADHD level exerted a smaller effect on reported language skills in children with above median IQ-score. The associations between ADHD symptoms and WM and response inhibition, respectively, were not influenced by IQ-score.
Rosenthal et al., 2013	CS; Clinical ASD (N=185). Examined EF in ASD from 5-7 y to adolescence	Four age groups: 5-7y, 8-10y, 11-13y, and 14-18y 83% total sample boys	Executive functions ("real world" EF, rated by parents).	ASD: ADI-R; ADOS; DSM-IV EF: BRIEF (8 scales: initiate, emotional control, shift, inhibit, organize/plan, organization of materials, working memory, monitor), collapsed into 2 broad indices: the behavioral regulation index and the metacognition index).	EF deficits increasingly appear with age. Shift scale of EF showed greatest problems at younger and older age. EF (particularly metacognitive abilities) in ASD matures at a slower rate than it does in typically developing children and thus shows greater divergence from normative samples with increasing age. Whereas flexibility remains particularly impaired across ages in ASDs, working memory, initiation,

					and organization, become increasingly problematic over time, according to parent report.
Schoemaker et al., 2012	CS; Clinical (N=2-2); ADHD (n=61), DBD (n=33), ADHD+DBD (n = 52); TD children (n = 56). Examine EF in children with a clinical diagnosis of ADHD, DBD and ADHD + DBD.	4.5y (3.5–5.5) % boys by group: TD=69.6 ADHD: 80.3 DBD=81.8 ADHD+DBD= 82.7	Executive function;	ADHD and DBD: CBE with CBCL; TRF; KDBS; DB-DOS; DSM-IV-TR; EF tasks: Inhibitory skills (Go-No-Go, Modified Snack Delay, and Shape School – Inhibit Condition) and WM tasks (Nine Boxes and Delayed Alternation).	Structure of EF: in the present sample of clinically diagnosed preschoolers, a two-factor model (inhibition and working memory) fit the data better than a one-factor model. Children with ADHD showed robust inhibition deficits, whereas those with DBD showed impaired inhibition especially where motivational incentives were prominent. Severity of inhibition impairment in the comorbid group was similar to the ADHD group. No between-group differences were found on the WM factor.
Skogan et al., 2013	CS; Population over recruited for ADHD (N=1045); control group (N=147) Investigated associations between ADHD symptoms and/or ODD and two EFs (inhibition and WM).	3.5y (SD=1.3) 53% boys	Executive functions: WM and inhibition	ADHD (3y): CBCL and DSM-IVTR ADHD diagnosis: PAPA EF: verbal WM: Stanford-Binet subtest "Memory for sentences", Block Span and Delayed Response; Nonverbal WM: visuospatial search task for preschool children; Inhibition: Statue subtest (NEPSY); IQ: SBIS.	The comorbid group (ADHD+ODD) was the only one separated from typically developing controls in terms of performance in both WM and inhibition. Symptoms of ADHD, both alone and with ODD, were associated with lower performance on tests of inhibition in the group comparisons. Dimensional analyses showed that performance within both EF domains contributed to variance primarily in ADHD symptom load. There was a small but significant association between symptoms of ADHD and lower WM performance. Effect sizes were generally small, indicating that measures of EF have limited clinical utility at this stage in development.
Smithson et al., 2013	CS; Clinical ASD (n=39) and typical control group (n=39) Examined executive control (EC) in preschoolers with and without ASD	4.4y (2.8-5.8) 82% boys	Executive functions ("real world" EF, rated by parents).	ASD: information from a detailed history, general observation; ADOS; DSM-IV EC: BRIEF IQ: WPPSI-R (1989) and WPSSI-III (2002)	Unlike many previous investigations of preschoolers with ASD, which failed to observe EC deficits on performance measures, we found pervasive EC deficits by parent report on a comprehensive, real world EC measure. (67 %) with ASD were rated by parents as having clinically significant EC impairments in one index from the BRIEF and a substantial minority (22 %) was elevated on all three index scores. There was no indication that preschoolers with ASD had relatively greater impairments in flexibility compared to other EC domains as hypothesized.
Yerys et al., 2007	CS; Clinical; Control. 1st experiment (N=54) included: ASD (n= 18), Developmental Delay (n=18); TYPically development (n=18).	Clinical: 2.9y (2.0-3.7); Control: 1.8y	Executive functions	ASD: combinations of ADI-R; ADOS-G; DSM-IV and previous/current ASD diagnosis; EF: Windows task (Russel et al. 1991); Spatial Reversal (Kaufmann et al. 1989); A-not-B (Griffith et al. 1999)	1st experiment: no specific EF deficits in ASD relative to MA-matched controls. 2nd experiment: similar EF abilities (measured by Windows and Spatial Reversal tasks) in ASD compared to CA-matched TYP in spite of significant differences in MA between the groups.

	2nd experiment (N=36) included: ASD (n=18) and typically development (n=18). Examined whether specific EF deficits are present in ASD and (2) whether such deficits are secondary to autism, or act as early cognitive risk factor for ASD by comparing EF abilities of this ASD group to a CA matched typically developing group.			IQ: MSEL	Overall, on EF measures children with ASD did not have a specific deficit in EF relative to either MA-matched control group; moreover, they did not exhibit a delay in EF abilities relative to the CA-matched typically developing control group. That is, our results demonstrate children with ASD perform similarly to CA and MA-matched children with DD and MA-matched typically developing children on almost all EF measures.

Key: Range*: If not reported, standard deviation (sd) is listed; Design: CS, cross sectional; LG, longitudinal; Clinical refers to a sample drawn from a clinical population; Population refers to a sample drawn from the general population; HR refers to high risk sample.
AD, attention deficit; ADHD, attention deficit/hyperactivity disorder; ASD, refers to autism spectrum disorder, autistic disorder, pervasive developmental disorder not otherwise specified (PDD-NOS) or Asperger syndrome; ALC, autistic like conditions; AP, attention problems; ATr, autistic traits; CBE, clinical best estimate diagnosis; CP, communication problems; DB(P)D, disruptive behavior (problems) Diagnosis; HI, hyperactivity/impulsivity; I, Inattention; RRBI, restricted repetitive behaviors and interests; SD, social difficulties.

Assessment instruments (as cited in the reviewed articles):
ADHD-RS-IV: ADHD Rating Scale IV (DuPaul et al. 1998);
ADI-R: Autism Diagnostic Interview-Revised (Rutter et al. 2003);
ADOS: Autism Diagnostic Observation Schedule (ADOS-G) (Lord et al. 2000) or (ADOS) (Lord et al., 2002);
BDI-2 :Battelle developmental inventory, second edition (Newborg, 2005);
BISCUIT-Part 1 and Part2: Baby and Infant Screen for Children with aUtIsm Traits (Matson et al., 2009);
BRIEF: Behavior Rating Inventory of Executive Function (Gioia et al., 2000);
Butterworth measure of joint attention. (Butterworth & Jarrett, 1991);
CBCL: Child Behavior Checklist 1 ½-5 years (Achenbach & Rescorla, 2000);
CBQ: Children's Behavior Questionnaire (Rutter et al., 1970);
CCQ: California Child Q-Sort (Block & Block, 1980);
CDI: Child Development Inventory (Doig et al., 1999);
CPC: Children's Problem Checklist (Healey et al., 2008);
CPRS-R :Impulsivity-Hyperactivity subscale of the Conners Parent Rating Scale-Revised (Goyette et al., 1978);
CPSCS: Social competence California Preschool Social Competence Scale (CPSCS) (Levin et al., 1969);
DB-DOS: Disruptive Behavior Diagnostic Observation Schedule (Wakschlag, Briggs-Gowan, et al., 2008; Wakschlag, Hill, et al., 2008)
DISCO_Diagnostic Interview for Social and communication Disorders (Wing et al., 2002);
ECBQ: Early Childhood Behavior Questionnaire (Putnam et al., 2006);
ECI-4: Early Childhood Inventory-4 parent and teacher versions (Gadow & Sprafkin, 1997, 2000);
FIST: Flexible Item Selection Task (Jacques& Zelazo, 2001);
IBQ-R: Infant Behaviour Questionnaire—Revised (Gartstein & Rothbart, 2003);
KDBS: Kiddie Disruptive Behavior Schedule (Keenan et al., 2007)

LABTAB: Laboratory Temperament Assessment Battery (Goldsmith et al., 2000);
M-CHAT (Robins et al. 2001);
M-P-R: Merrill-Palmer-Revised Scales of Development (Roid & Sampers, 2004)
MSEL: Mullen Scales of Early Learning (Mullen, 2005);
NEPSY: Neuro Psychological Assessment (Korkman, Kirk, & Kemp, 1998);
PAPA: Preschool Age Psychiatric Assessment (Egger et al., 2006) ;
PKBS: The Preschool and Kindergarten Behavior Scales (Merrell, 1994);
PLS-4: Preschool Language Scale, 4th Edition (Zimmerman et al., 2002);
RBS-R: Repetitive Behavior Scale-Revised (Bodfish et al. 1999, 2000);
SBIS: Stanford-Binet Intelligence scales, 5th edition (Roid, 2003);
SCDC: Social Communication Disorder Checklist (Skuse et al., 2005);
SCI: Social Competence Inventory (Rydell et al. 1997);
SDQ: Strengths and Difficulties Questionnaire (Goodman et al.,1997);
SIDAC: Structured Interview for Diagnostic Assessment of Children (Hynd, unpublished diagnostic interview, 1995;.
SRS: Social Responsiveness scale (Constantino, 2002).
TABV-R: Temperament Assessment Battery for Children-Revised (Martin & Bridger, 1998);
TOL: Tower of London
TRAILS-P: Trial Making Test for preschool children (Espy & Cwik, 2004)TRF: Teacher Report Form (Achenbach, 1991);
TRF: Child Teacher Report Form 1 ½-5 years (Achenbach & Rescorla, 2000);
VABS: Vineland Adaptive Behavior Scales (Sparrow et al., 2005);
WPPSI-R or WPPSI-III: Wechsler Preschool and Primary Scale of Intelligence (Wechsler, 1989; Wechsler, 2002)